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SPACE BIOLOGY AND AEROSPACE MEDICINE

No. 2, 1977

Complete translation of the Russian-language periodical
KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA
published in Moscow by the Meditsina Izdatel'stvo

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CURRENT STATUS OF SPACE BIORHYTHMOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 3-12

[Article by B. S. Alyakrinskiy, submitted 5 May 76]

[Text] One of the results of practical conquest of space is the significant revival of research in different branches of science, revision of many existing conceptions and formation of new scientific directions. Space biorhythmology, one of the branches of general biorhythmology, can be justifiably referred to these scientific directions; it has rapidly gained independent significance in the system of sciences that have the common objective of assuring man's prolonged existence in space.

Space biorhythmology was formed, so to speak, somewhat ahead of the practical tasks of maintaining in space man's initial system of circadian rhythm, the time sequence of cyclic processes developed in the entire course of evolution, which is a prerequisite for good health and efficiency. In the first brief space flights, the importance of preserving the body's biological rhythms could not yet be obvious to any extent. At that time, it was difficult to properly assess the role of the "biological clock" in the overall set of factors, upon which cosmonauts' health and efficiency depended. However, even at that stage of development of cosmonautics, some researchers called attention to some of the conditions of orbital flights which, a priori, could not be indifferent to the organism as a complex fluctuating system [51, 60, 67]. These referred, first of all, to the significant impairment of the system of constant time signals (timers [time sensors], the regulatory function of which on the ground is well known, with regard to man's circadian rhythms. For man, time sensors refer, first of all, to the numerous geophysical cycles generated by earth's rotation around its axis: day and night (lighting rhythms), daily fluctuations of air temperature, barometric pressure, humidity, intensity of magnetic and electrostatic fields of the earth, cosmic rays, as well as social cycles: work and free time, clock reading and that of other analogous instruments, radio and television receivers, etc. In an orbital flight, as we know, "day" and "night" follow one another at intervals of no more than 1.5 hours. There are no daily fluctuations and other geophysical time sensors. The social timers are impaired to some extent or other (primarily with regard to frequency of

display and intensity), and some are completely leveled off. Quite often, it is difficult to maintain a 24-hour daily cycle in orbital flight (due to decline and precession of the orbit, presence of so-called blind passes when radio communication with earth is interrupted, i.e., communication with flight observation centers), and for this reason the cosmonauts must adhere to a sleep and waking schedule of a shorter period (about 23.5-23.6 hours), so that the phases of such a rhythm are constantly shifting (migrating) in relation to the earth's time scale. Furthermore, for many reasons, lift-off time was often shifted to the night hours, and the cosmonauts had to postpone sleep to morning and daytime hours on ground elapsed time. Another reason for disruption of the customary daily sleep and waking cycle is that some of the operations to be performed by cosmonauts are strictly "tied" to specific ground time.

The potential hazard of disruption of circadian rhythms in view of the above distinctions of orbital flights was deemed to merit attention, in the light of data in general biorhythmology obtained from studies of the effects on man of changing latitudes [44, 55, 59, 48], working on evening and night shifts [6, 10, 11, 25, 30-33] and in the Arctic region [40, 61]. All of the studies demonstrated impairment of the initial state of the body, varying in degrees: sleep disorders, poor appetite and affect, impaired function of the gastrointestinal tract, neurotic symptoms and occasionally organic disease. According to the general opinion of biorhythmological specialists, the cause of these disturbances was desynchronization of circadian rhythms of the body, a shift in phase of these rhythms (for example, with regard to maximum or minimum intensity of different functions), as compared to the initial rhythm corresponding to an essentially healthy state. Such desynchronization of circadian rhythms (internal desynchronization) was due to a discrepancy between the phase of body rhythms and time sensors when changing latitudes, in the case of work in three shifts, etc. Some specialists considered expressly this to be the chief hazard of man's invasion of space. A. Brown [46] posed the question: "Would not the physiological transformations in living organisms, that are governed by a rhythm, fall into relative chaos rather soon, even if the cycles of illumination and temperature are carefully maintained?" And T. W. Hill [56] echoed his words: "In spite of the most optimistic dreams, man is not adapted to flights over several time zones, because of the great difference in time, or to flights in space, where there is a different day and night cycle" (p 380). G. T. Hauty [54] approached the same question from more pragmatic positions. Referring, in one of his works, to the prospects of manned space flights, he stressed the importance of considering the problem raised by the "biological 'day--night' rhythm," and he insisted on the need "to make a comprehensive study, under simulated space flight conditions, of the extent to which the 'day--night' cycle can be altered, from the standpoint of time, physiological functions and efficiency" in order to determine the extent of changes that can be made in this congenital limitation of man, without diminishing his functional capabilities. In the same work, G. T. Hauty submits the results of the first investigations of man's adaptation to unusual sleep and waking cycles: the subject could not adjust to a 4-hour work and rest shift for 7 days ("fatigue increased, efficiency

diminished and remained inadequate for most of the "flight"). After these studies (February 1958), many analogous experiments were conducted both in our country and abroad to determine the range of biorhythmological adaptability of man. In these experiments, which actually formed space biorhythmology as an independent scientific direction, studies were made of the distinctions of man's adaptation to days with a shift of phase [16, 19, 21, 24, 26], with complete inversion of phase [5, 13, 15, 18, 19, 29, 34, 35], to shorter and longer days [36, 37, 62, 70, 72], to days with a "split" sleep--wakefulness rhythm, i.e., alternation of sleep and waking periods every 4, 5 and 6 hours [14, 22, 23, 28], and to days with free [unrestricted] sleep and waking rhythm [27, 42, 45, 48, 63, 64, 69].

The late 1960's and early 1970's were a period of the most fruitful experimental work in this field, a period of accumulation of numerous data which, after comprehensive analysis, made it possible to formulate a number of theses that became part of the foundation of theory of space biorhythmology and are constantly used to offer concrete recommendations on organization of work and rest of cosmonauts. The most significant of these theses are: 1) man's adaptation to a sleep-waking rhythm with any (up to total inversion) shift in phase is possible, provided a 24-hour period is retained, and the effectiveness of such adaptation is related to existence of a positive set toward assimilating the new rhythm [17], meticulous adherence to the prescribed schedule [20], total reorganization of the entire system of time sensors (both physical and particularly social); 2) adaptation to phase-shifted rhythm is characterized by pronounced individuality: some individuals assimilate any phase shift with relative ease; for others, this process involves some difficulties and, finally, there is a certain group of individuals who experience great difficulties in such cases; 3) the change in rhythms of different functions takes place at a different rate, at different times: from a few days to a few weeks and months,* which is indicative of differences in inertness (lability) of biorhythms of the body. Apparently, the differences in lability of body rhythms are a manifestation of adaptation of the organism to the phenomenon of randomness (leveling off of the effect of random changes in time sensors). The body's time sensors respond to relatively brief disruptions by immediate reorganization of rhythms of only the functions that are primarily responsible for adequate behavior, and this provides satisfactory adaptation to altered living conditions for a certain time. And as soon as the original conditions are restored, the rapidly reorganized rhythms of highly labile functions (primarily the central nervous system) revert to their former state just as rapidly. The organism reacts to environmental perturbation with maximum economy [2]; 4) assimilation of a new living rhythm takes place in several stages, in view of the difference in lability of different functions. One of these stages is the stage of

*In the study of I. L. Vaysfel'd and R. F. Il'icheva [8], it was established that, 4 months after exposure to extreme factors, subjects presented overt impairment of circadian rhythm of biogenous amines of blood--histamine and serotonin, although they appeared well and there were no visible deviations referable to the cardiovascular and respiratory systems.

latent desynchronosis, when a state of subjective wellbeing and complete readjustment of rhythms of functional indices that are recorded the most frequently in experiments (pulse and respiration rates, arterial pressure, electroencephalogram, body and skin temperature, diuresis, mental productivity) is associated with incomplete readjustment of rhythms of other functions (excretion of potassium in urine [61]). The opinion is held that there is less resistance to deleterious factors in the presence of latent desynchronosis [3]; 5) it is impossible for man to adapt to 16- and 48-hour days. When attempts were made to obtain such adaptation (with strict adherence to living regimen), marked neurotic disorders developed, and these trials ended in failure; 6) adaptation to days lasting close to 24 hours (23 and 25 hours) present difficulties, with which not all subjects can cope (young people adjust better); 7) adaptation to "split" sleep and waking schedules is also not easy. Adaptation depends on how close the sleep period is to nocturnal hours on local time. The difficulties for the organism to adjust to shorter or longer days are an expression of the pattern established in the system of general biorhythmology: the more complex an organism, the more difficult to adjust to a rhythm, the period of which is significantly different from 24 hours; it is not easy for the human body to adjust to an artificial cycle that is shorter or longer than 24 hours [47]; 8) the system of circadian rhythms of the organism, when allowed to function freely, i.e., with maximum removal of all timers (including those that provide for an unregulated living schedule) is not very stable. J. Aschoff [43] stresses: "Various functions apparently represent different oscillators which are synchronized under normal conditions, but can become desynchronized when the rhythms proceed freely" (p 281).

Ground experiments have been the main source of facts characterizing the flexibility of the circadian system of the human body. Space flights, the duration of which has been constantly increasing, were another source. True, this source did not, nor could it actually yield facts in the amount, quality and sequence that would fully meet the requirements of scientific research on the problem of adaptation of man as an oscillatory system to spaceflight conditions. However, the data obtained from these flights were largely instrumental in defining a number of theses that were formed in space biorhythmology. Already during the flight of Vostok-2, thanks to the keen observations of G. S. Titov [39], data about the high "biorhythmological significance" were obtained. He was the one who noticed that, in orbit, the concepts of "day" and "night" were shifted to some extent, i.e., they lost their usual psychological meaning. This was the result of concrete physiological perturbations which, as we now know, consist of impairment of phasic architectonics of circadian rhythms. The sleep periods did not always coincide with night time hours at the spaceport during the orbital flight of the American astronauts, McDivitt and White (Gemini-4). The partial "loss" of sleep and lower efficiency of the astronauts was attributed to this, since these phenomena were not observed in the crew of Gemini-5, whose schedule provided for sleeping during the spaceport night hours.

Subsequent flights, made by both Soviet and American cosmonauts, particularly on the Apollo and Soyuz spacecraft, the Salyut and Skylab orbital stations, augmented significantly the amount of data of interest from the standpoint of biorhythmology. We submit some of them below.

Apollo-7: "Problems arose during this flight, which were related to major deviations from normal circadian rhythms in the crew. The crew reported sleeping poorly for the first 3 days of the flight."

Apollo-8: "The very full flight plan prevented simultaneous sleep and resulted in major deviations from normal circadian rhythm, thereby causing fatigue. The spacecraft commander experienced an actual shift of the circadian rhythm ranging from an 11-hour advance per phase to a 2.5 hour lag, as compared to the usual sleeping time on Cape Kennedy."

Apollo-9: "Deviations from the normal circadian rhythm resulted in some loss of sleep by the crew.... The crew experienced a shift in sleep periods, as compared to sleeping time on Cape Kennedy, which ranged from 3 to 6 hours."

Apollo-15: "During the translunar and transterrestrial phases of this flight, there was a minor shift, as compared to normal sleeping time on the ground. As a result, all of the crew members had a good sleep at this time." Different data were obtained during the expeditions on the moon: "The longer work period and shorter sleep periods on the moon resulted in severe fatigue, along with significant change in circadian rhythm of the lunar module crew, and served as the reason for working at the physiological limit until they returned to the command module."

During the flight of the Soyuz-9, the mild tendency toward slower heart rate in both crew members [7] was attributed to the full flight plan and "reversed" daily schedule. There is reason to believe that, in this same crew, development of fatigue was determined, to some extent, by migration of the sleep--wakefulness phase [9]. The change in daily schedule of the crew of the Salyut-4 station "had an adverse effect on some reactions of the body and was manifested, in particular, by sleep disturbances" and development of fatigue [12].

Thus, there are a number of facts indicative of the negative role of diverse disturbances of circadian rhythm in the course of actual space flights. At the same time, in the opinion of the authors who analyzed the results of the flight on the Skylab station, adherence to a customary living schedule reduced to a minimum the risk and hazard inherent in all space flights and aided in retaining good sleep [49].

Studies of adaptation to unusual daily sleep-waking rhythms of aircraft crews on transmeridional lines were very important to development of space biorhythmology. A. N. Nicholson [65, 66] analyzed the effects of such flights on pilots. He believes that adaptation to irregular ("split" type) sleep and waking schedules, which is typical in transmeridional flights, is basically possible and that expressly such schedules will be typical for future space flights.

The data obtained during the flight of the American Biosatellite-3 merit special attention, and their general biological importance is unquestionable. The circadian rhythms of a number of functional indices were recorded on monkeys on board this satellite and a few monkeys in chambers on the ground, where all of the flight conditions, except weightlessness, were simulated. It was found that there was no disruption of the indices recorded under ground conditions, whereas symptoms of desynchronosis appeared in the monkeys in orbit. Thus, the sleep-waking, arterial pressure, diuresis and urine creatinine rhythms retained their 24-hour duration, whereas the respiratory rhythm acquired a period of 25.5 hours, pulse rate--26 hours, body and brain temperature--26.5 hours and calcium excretion in urine--30 hours [53, 57]. The results of this experiment demonstrated the desynchronizing role of weightlessness, and added to the arsenal of its stressor effects on complex biological systems.

The desynchronizing effect of weightlessness is quite consistent with the facts already available, which were obtained in many experimental studies and clinical practice, indicating that impairment of the circadian rhythm of the body is a mandatory component of the general adaptation syndrome [1]. The thesis that desynchronosis is a mandatory component of the general adaptation syndrome promotes the problem of desynchronosis to the level of a central problem of space biorhythmology, since solution thereof is one of the main prerequisites for good health and high degree of efficiency of cosmonauts. In fact, prevention of desynchronosis, by virtue of the very substance of this problem, implies biorhythmologically substantiated regulation of the cosmonauts' life, rational organization of their work and rest. Theoretical and experimental works, particularly those pursued in recent years in the USSR, allow us to maintain that the basic principle involved in organizing a rational living schedule is the rhythm principle, and the rhythm must have a period of 24 hours [4]. This statement does not place a "ban" on the search for possible use in space of days lasting for a different period. In this regard, an interesting thought was voiced by S. I. Stepanova [38]. She attributes the role of regulator of duration of the circadian cycle to its informational and energy value, level of tension that is related to the amount of information processed per day and daily energy balance of the organism. If we accept the thesis that, in the course of the "work period" of his life, each man reaches and then maintains a certain, on the average rather stable level of tension for a long time, corresponding to the volume of daily flow of information and energy, we must agree that, with increase in intensity of this flow, the duration of the day should be reduced, and with decrease in this intensity, it should be extended. If the concept of information and energy value ["cost"] in its biorhythmological aspect will be confirmed (first of all, experimentally), the organizers of space flights will receive an effective means of controlling man's circadian rhythms and, consequently, of preventing desynchronosis. Here, it should be recalled that Ye. Ya. Shepelev [41] arrived at an analogous conception, but from very different positions. He believes that "under space flight conditions, the usual daily functional load of the body may be associated with less expenditure of energy, and this means less depreciation of mechanisms involved in converting the energy of nutrients into specific function of organs. Under

such conditions, either a shorter rest period or longer daily cycle as a whole would be acceptable. The latter should be considered preferable, since it retains the customary relationship between work and rest periods. As a result, we would extend flight days while retaining the customary relationship between sleep and waking on the ground, as well as expenditure of energy. In other words, we would have a functional equivalent of the usual rhythm of human vital activity, but it would be extended, as compared to ground elapsed time."

Investigation of the phenomenon of desynchronosis and research on means of prevention thereof enabled Soviet biorhythmologists to propose a system of measures to prevent desynchronosis in space (see Chart). Within the framework of this system, some promising investigations are planned, such as: a) the "loosening up" phenomenon, with reference to the usual regimen of vital activity before shifting to the variant of onboard days, which amounts in essence to attenuation of the initial organization of the circadian system by means of stressor factors (prolonged wakefulness, prolonged sleep, etc.); b) "inculcation" of new sleep--waking rhythm by means of numerous preliminary transitions to the onboard day variant; c) biorhythmological screening of candidates for extensive space flights. In 1974-1975, work in the last mentioned direction was done by S. I. Stepanova, and she concluded that there is a correlation between biorhythmological adaptability (to a shift of the sleep--waking phase within the framework of a 24-hour day) and constancy of circadian rhythms (stability of their parameters for at least 10 observation days). In turn, the constancy of circadian rhythms is most completely characterized by stability of the position of the acrophase (maximum or minimum of the circadian rhythm curve) on the time axis. In spite of the fact that these are only preliminary conclusions, it is quite obvious that this is a promising direction in biorhythmological research.

Work dealing with methodology of space biorhythmology merits special attention, although, of course, such work is equally important to general biorhythmology. But it is expressly space biorhythmology that induced development of such research, since it became, for a while (late 1960's), the arena of bitter debates as to its place and importance in the system of sciences called upon to assure the safety and effectiveness (from the standpoint of the human element) of space flights serving different purposes. In this regard, it is deemed particularly important to substantiate the universality of biological rhythms and significance, in particular, of circadian rhythm. Theoretical research in this direction revealed that the biological rhythm is an expression of unity and conflict of opposites in the realm of living matter, that the "biological rhythm is characterized by continuous disruption and restoration of the original state which, however, upon the closest scrutiny, is found to be a certain new state" and, consequently, that the "biological rhythm is a property of living systems, their inherent internal movement, with returns to the starting points, each of which is, in actuality, both the same and different, i.e., movement over a spiral governed by the law of negating negation" [4, pp 41-42]. For expressly this reason, when we now refer to manned space flights, we cannot fail to take into consideration this rhythm and its effect on all physiological functions of man, including efficiency [43].

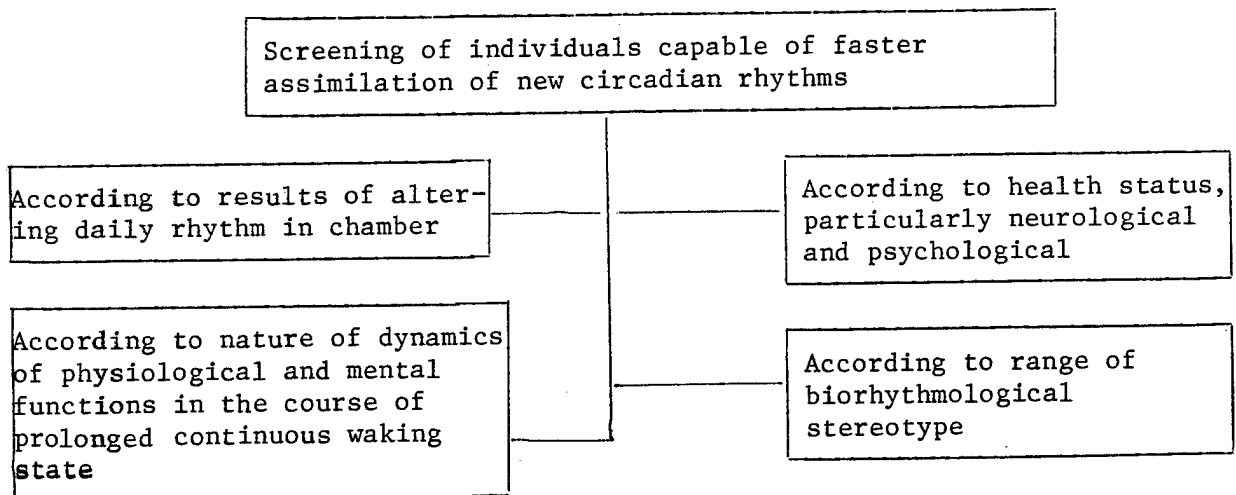
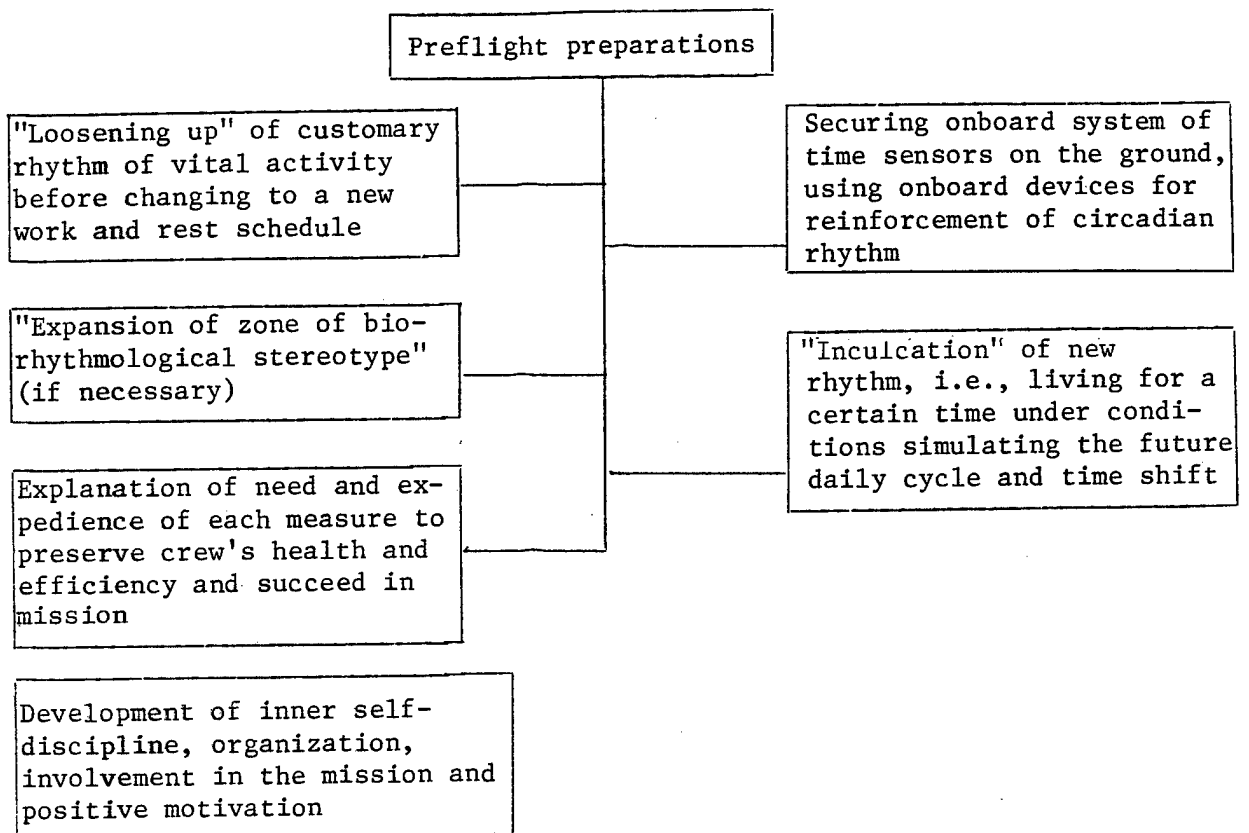


Chart [Part 1]
System of measures to alleviate readjustment and maintenance of man's biological rhythms in the course of prolonged space flights

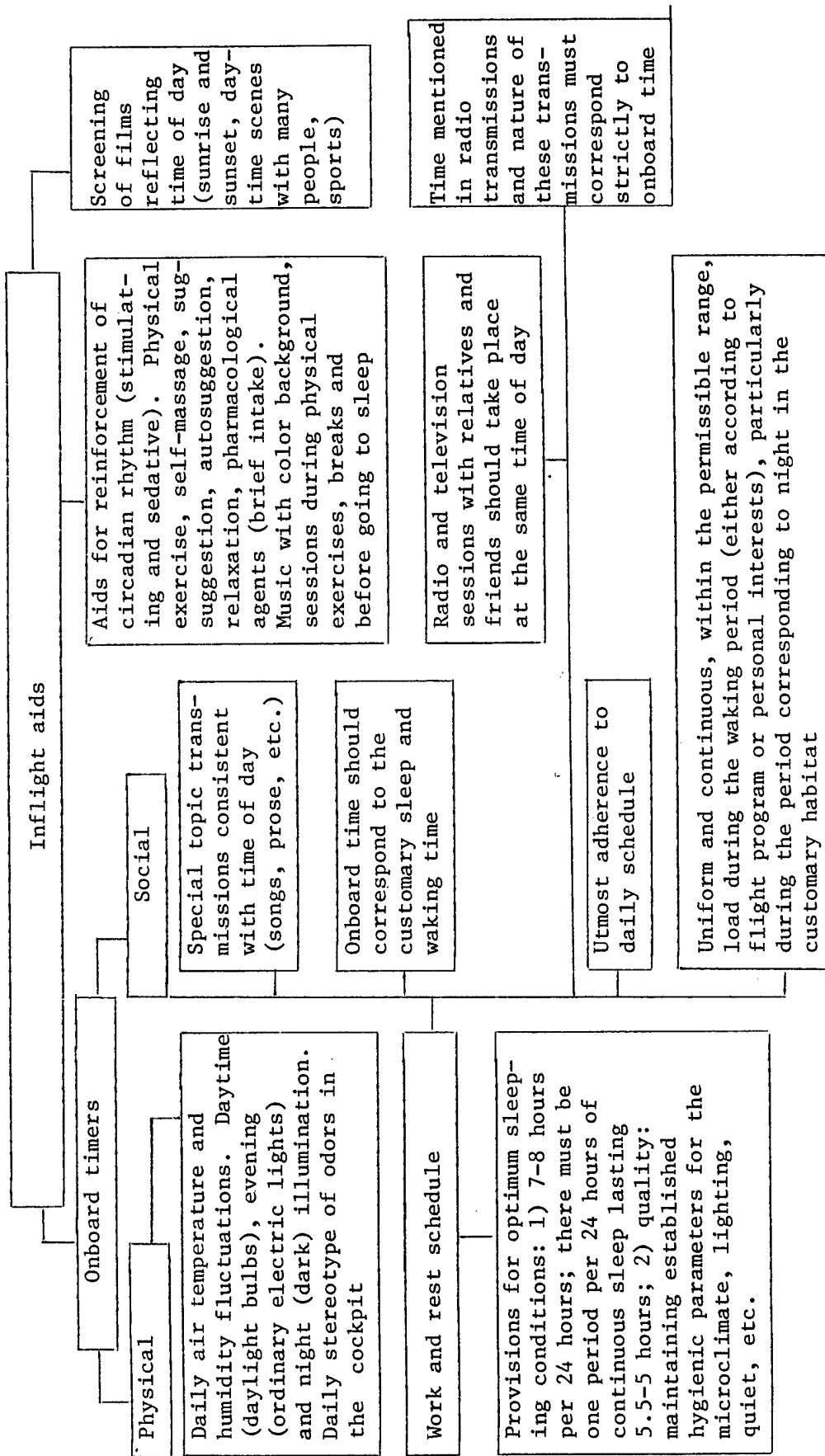


Chart [Part 2]

At the present time, space biorhythmology has gained broad recognition and proper understanding of its place in the system of sciences united within the framework of space medicine. According to reports in the American press, representatives of NASA and other scientists have voiced the following views to the subcommission for space research: there are two biological problems that should be considered first and foremost: the biological effects of weightlessness and altered circadian cycle [50]. F. Halberg et al. [50] write: "Manifestation of stability of rhythms in astronauts stresses the need for continued work ... to define control of rhythmic factors, which influence not only the long-term schedule of man's activity in space flights, but rhythmic behavior of the organism of sick people as well. It remains mandatory to implement such research, by means of precise evaluation of circadian and other parameters on the ground. But, even with availability of such base information, the problem of biorhythms of the human body in near-earth and near-moon orbital, as well as interplanetary flights, is still one of the principal ones in the United States program of space research. Solution thereof will serve as fertile soil for future international collaboration, including research on other issues directly related to efficiency and endurance of the human body" [52].

" Special attention should be given to manifestation of signs indicative of the influence of the environment on circadian rhythms, in future space flights" [58].

Any progress on the road of theoretical and experimental research in the field of biorhythmology serves the cause of conquering space.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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BIOMEDICAL RESEARCH ON THE PROBLEM OF ARTIFICIAL GRAVITY

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[Article by A. R. Kotovskaya, R. R. Galle and A. A. Shipov, submitted
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[Text] Weightlessness occupies a special place among space flight factors. Before the first manned flights into space, it was expected that cosmonauts could develop the most diverse disorders under weightless conditions. However, the gloomiest of the predictions were dispelled after studies were made of the effects of weightlessness on the animal and human organism in a series of experiments on geophysical rockets, biological satellites and spacecraft.

Indeed, the experience of Soviet and American cosmonauts is convincing evidence of the possibility of man's rather long existence in weightlessness. The level of efficiency required to fulfill the flight mission persisted in flights lasting up to 3 months [5].

However, the results of the biomedical studies pursued in space do not offer conclusive enough grounds to predict that flights of any duration would be safe to human health.

At the same time, extension of manned space missions from a few months to a few years is one of the chief directions of development of cosmonautics. We refer, first of all, to flights in a near-earth orbit, flights to the moon and, finally, to planets in the solar system.

The most substantial limitation of flight duration is the need to protect man from the deleterious effects of prolonged weightlessness, as well as the difficulties involved in organizing housekeeping facilities and efficient cosmonaut performance in weightlessness. In other words, in view of the prospect of extending space expeditions, the urgency and importance of the "man and weightlessness" problem are not only diminishing, they are even increasing.

The space flights in the Salyut and Skylab orbital stations revealed that man tolerates weightlessness lasting up to 3 months relatively well, and retains a high enough level of efficiency. At the same time, the changes observed in the cosmonauts (lowering of orthostatic stability, deterioration of locomotor system) could not be completely eliminated by the preventive measures taken (physical exercise, negative pressure to the lower half of the body, pharmacological agents, etc.). Furthermore, these preventive measures made it difficult to organize housekeeping facilities and comfortable rest for the cosmonauts, and they took up much of the crew's time.

The flights in spacecraft and orbital stations also revealed that, with increase in duration of flights, there is an increase in time assigned for preventive measures. One could hardly consider this a beneficial tendency, since it reduces the time for rest and useful activity of cosmonauts.

Finally, the efficacy of the preventive measures used has been defined only with reference to flights of immeasurably shorter duration than would be required in flights to planets in the solar system.

For this reason, development of means of preventing the deleterious effects of weightlessness which, on the one hand, would be effective and safe to health whatever the duration of a flight and, on the other hand, would not be burdensome to the spacecraft crew should be considered one of the focal tasks for space medicine.

The creation of artificial gravity (AG) by rotating a spacecraft may be the most adequate means of solving this problem [7].

AG eliminates the weightlessness factor proper, rather than the different manifestations of its adverse effect on the organism. The influence of artificial "weightiness" extends to all systems of the organism, so that there are grounds to consider it the most universal preventive measure. AG relieves the cosmonaut from performance of a set of other preventive measures, which take up more time, with increase in duration of the flight. Finally, AG eliminates a number of housekeeping inconveniences due to weightlessness: pollution of the cockpit atmosphere by fine dust particles, difficulty of taking food and using water, etc. On the whole, AG renders living and working conditions of cosmonauts close to the customary ones on the ground, and this is rather important in long orbital and interplanetary flights.

From the biomedical point of view, the main aspect of the AG problem is to determine the desirability of AG in long space flights and to select the optimum parameters of AG. The basic question of necessity of AG is being answered as experience is gained in long flights under weightless conditions.

AG, which occurs as a result of rotating a spacecraft around the mass center, contributes a number of factors, the effects of which on the human body have not yet been adequately investigated.

In addition to the centripetal acceleration that generates AG, in a rotating space system man is exposed to concomitant factors: precession accelerations, Coriolis forces and the AG gradient [6, 14, 16-19].

Probably, it will be possible in the future to develop space objects with AG, in which the concomitant factors will be so infinitesimal, that man will not feel them. But this will require the building of spacecraft with a very wide rotation radius. Thus, with a rotation radius of 900 m and angular rotation velocity of 1 revolution/min, the AG equals that of the earth and concomitant factors are minimal, so that man would apparently feel just as he would on the ground.

Lowering the required level of gravity simplifies considerably the technical implementation of the idea of creating AG by means of rotation. For this reason, the central objective of biomedical research on AG is to determine the minimum centripetal acceleration, long exposure to which in flight would not be associated with the deleterious effects of weightlessness.

The first work dealing with experimental physiological substantiation of minimal AG level required to maintain normal posture and coordination of movements was done by Ye. M. Yuganov et al. on animals [8, 9]. Subsequent research of Soviet and foreign authors confirmed that AG of 0.28-0.35 G prevents motor disturbances in animals. In the presence of 0.5 G gravity, the nature of locomotion of man does not differ from the natural one [10]. However, one should not overlook the fact that the works mentioned were pursued in the case of brief weightlessness during flights in aircraft. The findings require verification, as they apply to man's performance in a prolonged space flight.

The main physiological criteria of adequacy of the selected AG for man should apparently consist of the following: function of the cardiovascular system and locomotor system, as the most vulnerable systems in the presence of weightlessness.

During space flights with artificial gravity ["weightiness"], cosmonauts will be exposed to concomitant mechanical forces (accelerations), due primarily to their movements in the rotating system.

In the case of linear movements of man in a rotating system, he will be exposed to Coriolis accelerations. Coriolis accelerations make it difficult to coordinate movements while walking, moving radially, as well as carrying weight, hammering in nails, decanting fluids, getting up from a chair and jumping [16]. Coriolis accelerations are the cause of some visual illusions and, when they recur they could cause development of motion sickness [4, 16, 18]. Coriolis accelerations affect the proprioceptors of the human body and otolithic receptors of the vestibular system.

The accelerations that occur with angular movements within a rotating system are called precessional, and they are angular accelerations [4, 6]. Additional exertion is required on space stations with AG to turn objects

outside the plane of rotation of the station, as well as to retain the usual trajectories of arm and leg movements [19]. In this case, the precessional accelerations affect the body's proprioceptors.

When the head is rotated about axes that are not parallel to the axis of rotation of the station, a different pattern of stimulation of receptors of the semilunar canals of the vestibular system, as compared to natural conditions, will be created due to appearance of precessional accelerations [4, 6]. Information is delivered to the central nervous system about a head movement that does not correspond to a real turn and contradicts the visual and proprioceptive information about the performed movement, and as a result there may be spatial disorientation, undesirable compensatory body movements, motion sickness and general malaise [12].

A number of ground-based investigations have been pursued by Soviet and foreign authors [2, 4, 11], dealing with the effects on the human body of prolonged (up to 1 month) stays in a rotating system.

As a result of the studies, it was established that it is possible in principle, for man to exist in an object that rotates at a constant angular velocity. Efficiency is retained and there are no health-endangering disturbances.

With angular velocities of up to 3 r/min, there are virtually no disturbances referable to man's general condition and efficiency. In the range of 3 to 6 r/min, at the first stage of rotation, disturbances arise with reference to postural equilibrium and symptoms of motion sickness, the severity of which is directly related to magnitude of angular velocity. It is important to stress that, with such rotation velocities, adaptation develops by the 6th-8th day, and subsequent presence in the rotating system is characterized by a normal general condition and efficiency.

Adaptation to rotation at velocities in excess of 6 r/min occurs only if special measures are used, such as gradual [in steps] progression of the system to the specified velocity of rotation, screening of individuals who are particularly resistant to vestibular factors, preliminary conditioning, intake of pharmacological agents against motion sickness, etc.

Thus, as a result of ground-based experiments lasting up to 1 month, it was established that the rotation factor could not serve as an obstacle, from the biomedical point of view, to developing space objects with AG.

At the same time, there are rather justified assumptions that, with an AG level below earth's gravity, there may be a change in sensitivity of the vestibular and motor analyzers to adequate stimuli [3]. For this reason, systematic investigation of the distinctions of man's vital activity in a rotating spacecraft at different AG levels, as well as the search for means of averting adverse reactions occurring at the first stage of rotation should be the logical continuation in the direction of research we are discussing.

With decrease in rotation radius of a spacecraft, there is increase in the AG gradient, which is characterized by the magnitude of the ratio between gravity at the floor level (feet) and head. Since the magnitude of the gradient depends on the relationship of a man's height to the spacecraft rotation radius, the gradient is often expressed by this ratio, as a percentage. This index constitutes 100% when the radius of rotation of the craft equals a man's height.

At the present time, there are no experimental data concerning man's endurance of a gravity gradient in the case of gravity below that of earth. The physiological significance of the gravity gradient can only be determined in a space flight, through studies on man, involving changes in the radius of rotation.

The use of onboard centrifuges with a short radius merits special investigation. The practical significance of such a centrifuge, in the light of the AG problem, has not yet been established, but from a technical point of view such a centrifuge may be acceptable for creating brief periods of increased "weightiness" at different stages of a space flight.

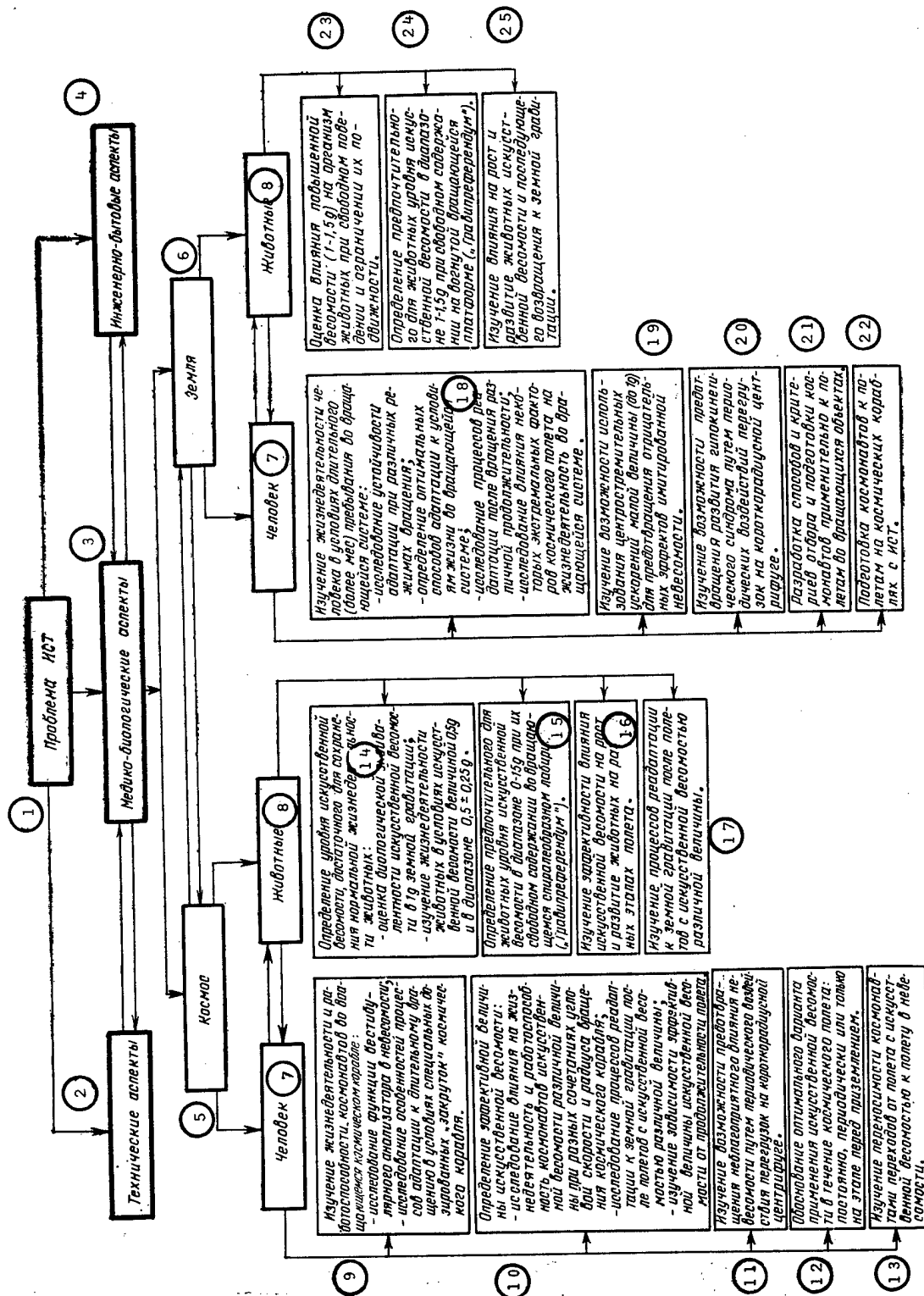
Some of the basic problems of AG can be resolved through flight experiments with animals. Animal experiments make it possible to perform procedures and studies that cannot be done on man, and they make it possible to demonstrate statistically reliable tendencies in a single flying expedition. Unquestionably, there is only limited possibility of direct extrapolation of the data obtained to man. This applies, in particular, to questions related to the effects of weightlessness on the cardiovascular system, physiological effects of precession and Coriolis accelerations, etc.

Animal experiments can solve problems such as substantiation of AG as a means of preventing the deleterious effects of weightlessness, definition of the magnitude of artificial gravity ["weightiness"] selected for man, determination of possibility of vital activity of living organisms in spacecraft rotating for long periods of time, etc.

Among the pressing problems that could be resolved in animal experiments, the first and foremost ones are evaluation of biological equivalence of earth's and artificial gravity and obtaining data on the possibility of preventing the deleterious effects of weightlessness by means of AG.

The presence of the rotation factor and AG gradient in relation to different parts of the animal body does not yet warrant the statement that AG is biologically equivalent to earth's gravity. It would be desirable to explore this question, which is important to the AG problem, by means of experiments on small laboratory animals, using an onboard centrifuge installed on a biological satellite.

Long-acting accelerations of 1 G can be created by a centrifuge. The animals are placed at the tip of the centrifuge radius, and the control group, outside the centrifuge. Ground-based control experiments, including rotation of animals on a centrifuge with minimal radius ("nonradius" centrifuge) permits evaluation of the importance of the rotation factor, as well as other flight factors associated with the experiment.



[Key for this chart is given on the following pages]

Main directions of research on the problem of artificial gravity (AG)

Key to chart on p 20:

- 1) the AG problem
- 2) technical aspects
- 3) biomedical aspects
- 4) engineering and housekeeping aspects
- 5) space
- 6) earth
- 7) man
- 8) animals
- 9) investigation of vital functions and efficiency of cosmonauts in a rotating spacecraft, studies of: vestibular analyzer function in weightlessness; distinctions of processes of adaptation to prolonged rotation with exposure to special, measured "spins" of spacecraft
- 10) determination of effective level of AG, studies of: effects on vital functions and efficiency of cosmonauts of AG varying in magnitude, with different combinations of angular velocity and radius of spacecraft rotation; processes of readaptation to earth's gravitation following flights with various levels of AG; relationship between efficacy of magnitude of AG and duration of flight
- 11) investigation of possibility of preventing the deleterious effects of weightlessness by means of periodic exposure to accelerations on a short-radius centrifuge
- 12) substantiation of optimum variant of use of AG during space flight: continuous, periodic, or only at the prelanding stage
- 13) investigation of endurance by cosmonauts of transitions from flight with AG to flight in weightlessness
- 14) determination of level of AG adequate to preserve normal vital functions of animals: evaluation of biological equivalence of AG of 1 G to earth's gravity; investigation of vital functions of animals exposed to AG of 0.5 G and in the range of 0.5 ± 0.25 G
- 15) determination of level of AG preferable for animals in the range of 0-15 G when they are unrestricted in a rotating spiral maze ("gravipreferendum")
- 16) investigation of efficacy of the influence of AG on growth and development of animals at the early stages of flight
- 17) investigation of processes of readaptation to earth's gravity after flights with different magnitudes of AG
- 18) investigation of human vital functions during a prolonged stay (over 1 month) in a rotating system, studies of: stability of adaptation with different modes of rotation; optimum means of adaptation to living conditions in a rotating system; processes of readaptation after rotation for different periods of time; effects of some extreme factors of space flight on vital functions in a rotating system
- 19) investigation of the possibility of using centripetal low-level accelerations (to 1 G) to prevent the adverse effects of simulated weightlessness
- 20) investigation of the possibility of averting development of the hypokinetic syndrome by means of period exposure to accelerations on a short-radius centrifuge
- 21) development of means and criteria for screening and training cosmonauts for flights in rotating objects

Key to chart on p 20 [continued]

- 22) training cosmonauts for flights on spacecraft with AG
 - 23) evaluation of effects of increased gravity (1-1.5 G) on the animal organism, as related to unrestricted behavior and limited mobility
 - 24) determination of preferred level of AG for animals in the range of 1-1.5 G when they are kept unrestricted on a concave revolving platform ("gravipreferendum")
 - 25) investigation of the effects of AG and subsequent return to earth's gravity on growth and development of animals
-

The criterion for evaluation of experimental results may be a set of physiological, biochemical, morphological, histochemical and other indices, with reference to which the most distinct adverse effects of weightlessness, without the use of preventive measures, are demonstrable.

Of interest are experiments with AG of 1 G on biological objects that have been used repeatedly in space flights. Such an experiment was conducted with some of them on the Kosmos-782 satellite (1975). In particular, such an experiment on biological objects, for which earth's and artificial gravity are equivalent, would permit differentiation between changes attributed to weightlessness and effects of other factors of space flights.

Experiments with small laboratory animals do not permit determination of one of the important AG parameters: maximum permissible angular velocity of rotation, in view of their low degree of sensitivity to motion sickness. At the same time, there is reason to assume that the minimum permissible AG levels will be similar for all mammals. The relatively high resistance of small laboratory animals to vestibular factors permits more precise evaluation of the minimum level of gravity. Furthermore, this permits increasing appreciably the velocity of rotation and, consequently, reduction of centrifuge size.

In this connection, a "gravipreferendum" experiment would be very important to determine on animals the preferred level of AG over a range including low gravity, when the animals are given freedom of choice.

It has been shown in ground-based experiments that animals always move in the middle of a rotating centrifuge, i.e., in the region of the minimum gravity on earth (1 G), regardless of velocity of rotation. Consequently, the animals usually perceive higher gravity as an unpleasant stimulus. Still unclear is the reason why the animals move to the area with the lowest gravity (1 G): Is it because they developed under earth's gravity, or because they prefer, in general, lower gravity? In other words, it is necessary to determine whether the animals would choose the area with AG of less than 1 G if they were given an opportunity to do so.

Such an experiment is feasible, for example, if a device is used that consists of a spiral maze with vertical walls placed on a centrifuge [15]

installed on a biological satellite and rotated at a constant velocity. The inner surface of the wall of the spiral would serve as the floor for the animals during a space flight. As they move through the maze, the animals could choose the optimum ("comfortable") level of AG ranging, let us assume, from 0 G in the center of the spiral to 1.5 G on the external twist.

There are also other possible designs [13] for a device to be used in a biological "gravipreferendum" experiment.

We have reason to believe that, for the first days of the flight, the preferred level of gravity will be close to earth's [13]. With increase in duration of weightlessness, the preferred level of AG will probably decline and then become stabilized at under 1 G [15]. Probably, this could be considered the minimum permissible gravity level for mammals, including man.

Thus, to solve the AG problem, a broad set of studies must be conducted, both with the participation of man and in experiments on animals [1]. The chart illustrates the principal directions of research on AG and biomedical problems that have yet to be solved.

The ultimate goal of biomedical research on the AG problem is to determine the minimum magnitude of centripetal acceleration sufficient to assure normal vital functions and efficiency of cosmonauts in the course of lengthy space expeditions, as well as to choose the optimum relationship between magnitude of radius and angular velocity of rotation of a space system.

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RESULTS OF CLINICAL EXAMINATION OF COSMONAUTS FOLLOWING A 63-DAY FLIGHT

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[Article by A. V. Beregovkin, T. N. Krupina, G. D. Syrykh, M. M. Korotayev, N. A. Kuklin, V. A. Balandin, V. S. Znamenskiy, V. I. Nikiforov, V. V. Nistratov and V. D. Portnov, submitted 20 Feb 76]

[Text] Cosmonauts P. I. Klimuk and V. I. Sevast'yanov, who made the 63-day flight, were already familiar with the sensations arising under the influence of weightlessness, since they had participated in a space flight before, although they perceived these sensations differently. Thus, for the 1st hour of flight, P. I. Klimuk had the sensation of having his body turned over. His general wellbeing was good on the 1st day of weightlessness. For the next 2 flight days, there were vestibular disorders and lack of appetite. In his first flight, high spirits lasted for 4-5 hours after P. I. Klimov became weightless. The sensation of being turned over persisted for 1.5 days and the vestibular disorders, for 3 days.

V. I. Sevast'yanov had the sensation of blood rushing to his head and a stuffy nose when he became weightless, in both the first and second flights. The sensation of blood rushing to the head regressed only after 10 days. Both cosmonauts presented some swelling of the face, narrow eyeslits and disappearance of wrinkles from the face.

The period of adaptation to weightlessness lasted about 8 days. However, the cosmonauts' efficiency remained quite high at all stages of the flight. There were no diseases whatever during the flight. P. I. Klimuk experienced mild, gnawing muscle aches in the lumbar region throughout the flight, and they disappeared after he returned to earth. Both cosmonauts had the sensation of dry plantar surfaces of the feet during the flight. EKG recorded on different flight days showed some changes: moderate shortening of the atrioventricular and extension of intraventricular conduction, with decreased amplitude of T waves. Periodically, there were isolated ventricular extrasystoles on the EKG of V. I. Sevast'yanov. In some cases, the appearance of extrasystoles could be related to emotional tension.

At the final stage of the flight, the cosmonauts tolerated accelerations well. The landing was soft. Immediately after landing, both reported the

sensation of increased weight of the body and objects around them. According to V. I. Sevast'yanov, it corresponded to about 2.5 units. P. I. Klimuk reported that he felt "all the fluid moving from the head downward, to the feet." The sensation of high weight [gravity] persisted for 2 days. When checked at the landing site, pulse rate, in supine position, was 90 for P. I. Klimuk and 80/min for V. I. Sevast'yanov. When they changed to vertical position, it changed to 120 and 128/min, respectively.

Both cosmonauts experienced general weakness, rapid fatigability, shaky and unstable gait. There was pallor of the integument and visible mucous membranes, signs of stasis in the gingival papillae and margins of the gums, against the background of slightly anemic mucosa, with gingival papillary bleeding and deposition of subgingival and supragingival tartar.

After thorough removal of tartar and anti-inflammation therapy, these symptoms disappeared within 4 days.

The nasal conchae were swollen in V. I. Sevast'yanov, and both cosmonauts presented some dryness of the nasal mucosa. We were impressed by diffuse hypotrophy of muscles of the lower limbs. As compared to preflight data, the perimeters of symmetrical parts of the limbs decreased: the arm by 1 cm, thigh by 3.7 cm and leg by 3.6 cm in P. I. Klimuk; the thigh by 0.7 cm and leg by 1.8 cm in V. I. Sevast'yanov. Palpation, as well as myotonometry, revealed diminished muscle tone. Thus, there was a decrease by 6 arbitrary units in tonus of the biceps of the arm of P. I. Klimuk, and by 10 arbitrary units in V. I. Sevast'yanov; the decreases in tonus of the femoral quadriceps constituted 7 and 9 arbitrary units, respectively. While the tonus of the brachial biceps was restored on the 2d-3d day, that of femoral muscles was restored on the 7th, while recovery of circumferences of the limbs occurred in the 3d-4th week.

P. I. Klimuk weighed 3.8 kg (5.3%) less, and regained the weight on the 13th day. After the first 8-day flight, he also lost 5.6% of his body weight and recovered it on the 9th day.

In V. I. Sevast'yanov, weight loss constituted 1.9 kg (2.8%) and he regained it on the 2d day. After the 18-day flight, weight loss constituted 5.6% with restoration on the 20th day.

Lymph nodes, thyroid and heart outline showed no changes. Heart sounds remained clear and resonant. Auscultation revealed vesicular breathing and no rales. For the first 14 postflight days there was a tendency toward tachycardia and lability of pulse, related to position of the body. Arterial pressure was slightly elevated, particularly diastolic.

The EKG taken after the flight showed negligible decline of T wave voltage in all leads.

The abdominal organs showed no distinctions. The tongue was moist and clear. There were no physiological disturbances.

Neurological examination revealed a shaky, unstable gait with lateral deviations in Romberg's position; tremor of extended fingers; some accentuation, for the first few days, of tendon and periosteal reflexes, equal on both sides; depression of abdominal reflexes. For the first 2-3 days, P. I. Klimuk presented nystagmoid twitching of the eyeballs in extreme positions.

Mild hyperemia of the conjunctiva of the lids and sclera was observed in both cosmonauts after landing. It disappeared in 1 day in P. I. Klimuk and on the 3d day in V. I. Sevast'yanov. On the 1st day after landing, both cosmonauts presented moderate dilatation of retinal veins. Visual acuity was diminished by about 0.1. Acuity was restored on the 7th day in P. I. Klimuk and on the 3d day in V. I. Sevast'yanov.

Of some interest is the syndrome of vestibular instability, which developed in P. I. Klimuk 2 hours after the flight. It was characterized by vertigo, mild nausea, unpleasant sensations in the epigastric region, pallor and perspiration of the integument when making quick turns and rotating the head. He had no appetite. Intake of plavagin tablets improved his condition appreciably. Such signs lasted 1.5 days and disappeared abruptly after the 2d night's sleep.

On the 1st day after landing, peripheral blood revealed some decrease in number of erythrocytes, reticulocytes, thrombocytes and hemoglobin. Tests made on the 7th day revealed an increase in reticulocytes and erythrocytes. The thrombocyte count remained at its former level, while hemoglobin continued to decline. Urinalysis failed to demonstrate any appreciable deviations; however, there was more intensive excretion of urates and phosphates, as well as albuminuria of 0.025 % in P. I. Klimuk and 0.035 % V. I. Sevast'yanov.

Functional load tests (LBNP [lower body negative pressure], passive anti-orthostatic, exercise tolerance test on a bicycle ergometer) on the 1st, as well as 3d and 7th days after landing, were tolerated satisfactorily by both cosmonauts, according to their subjective evaluation; however, there was an intensive reaction in the cardiorespiratory system. Isolated extrasystoles were recorded in P. I. Klimuk during the exercise test on the ergometer and in V. I. Sevast'yanov during the orthostatic test.

Thus, the clinical examination of the cosmonauts revealed that a 63-day exposure to weightlessness did not elicit pathological changes in the body.

In the course of the long space flight, the cosmonauts presented the same functional changes as in the first, shorter one, due to redistribution of blood. There was significantly easier adaptation to weightlessness, according to subjective evaluation. There was no appreciable difference in amount of weight lost by P. I. Klimuk, as compared to the 8-day flight, whereas it was 50% less in V. I. Sevast'yanov. The weight was regained on the 2d day after landing, and after the 18-day flight, on the 20th day.

According to the postflight physical examination, the following functional changes were demonstrated in the cosmonauts: general asthenization with signs of vegetovascular instability; sensorimotor and statokinetic disturbances; moderate dystrophy of muscles of the lower extremities; some depression of hemopoiesis.

These functional changes were reversible, and they were much milder in V. I. Sevast'yanov than after his 18-day flight. The recovery period was not associated with any complications, in both P. I. Klimuk and V. I. Sevast'yanov.

The following measures were implemented during the period of readaptation to earth's gravity: strict adherence to a program of motor activity with gradual expansion thereof, mandatory bedrest after each meal, proper vitamin supplements in food, therapeutic massage and therapeutic physical culture.

ELECTROGRAPHIC EXAMINATION OF THE CREW ON THE SECOND EXPEDITION OF SALYUT-4

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[Article by M. M. Korotayev, I. I. Popov, V. A. Degtyarev, Z. Z. Dorofeyeva, A. D. Yegorov, V. V. Kalinichenko, S. I. Ponomarev, V. P. Sidorov, A. P. Polyakova, Z. A. Golubchikova and A. A. Savilov, submitted 5 May 76]

[Text] Man's participation in long orbital flight may be associated with impaired regulation of cardiac activity and decreased reserve capabilities of the heart in the presence of functional loads. On the EKG, these changes are manifested in the form of sinus arrhythmia, bradycardia, extrasystole, atrioventricular rhythm at rest and with a load, etc. Signs of diminished myocardial contractility were demonstrated in some cosmonauts submitted to functional tests after landing.

As a rule, special leads were used to record, until recently, EKG's in flight, which permitted operational monitoring of the cosmonauts' condition, but yielded only limited information concerning bioelectrical activity of the heart. In this work, we submit the results of analyzing EKG's taken on cosmonauts during and after a prolonged orbital flight, using both DS leads and the classical leads used in clinical practice.

Methods

The EKG was recorded both at rest and while the cosmonauts performed functional tests on a bicycle ergometer with loads of 350-450 kg-m/min lasting 5 min. The EKG was recorded in the 12 classical leads on the 5th, 31st, 46th, 50th and 60th days of the flight, and on the 14th, 22d, 37th and 53d days (on the days of the functional tests) on an abbreviated program using some of the standard or chest leads. In addition, the EKG was taken in the DS lead once every 2 days. The technique for taking an EKG in space flight was virtually no different from the one used in the practice of clinical medicine. EKG studies on this scale were first made during the flight of the Salyut-3 orbital station, then continued on the Salyut-4 station. Polinom equipment was used to record the EKG; it permitted synchronous recording of 3 EKG leads, calibration of the signal, transmission of data over telemetry channels and recording on the onboard magnetic tape storage

unit. The quality of the EKG tracings was quite consistent with current clinical requirements. However, the bulk of the material was transmitted over the telemetry channels, so that some tracings (particularly during performance of physical exercise) could not be interpreted completely.

Results and Discussion

In both P. I. Klimuk and V. I. Sevast'yanov, the preflight bioelectrical activity of the myocardium showed no appreciable deviations from normal; both cosmonauts only presented isolated extrasystoles, which were recorded during some studies at rest and during the load tests.

In flight, the rhythm of cardiac contractions was constantly sinusoid, correct, with moderate sinus arrhythmia in P. I. Klimuk. During the period of putting the spacecraft in orbit, as well as during flight, we recorded some extrasystoles in V. I. Sevast'yanov; their appearance was usually preceded by emotional or physical tension.

After the flight, extrasystoles were observed in both cosmonauts: isolated or double supraventricular extrasystoles on the 3d postflight day during the physical exercise test on the bicycle ergometer (650 kg-m/min for 7 min) in P. I. Klimuk; isolated atrioventricular extrasystoles during the anti-orthostatic test on the 1st, 3d and 7th postflight days in V. I. Sevast'yanov.

The inflight time parameters of the EKG did not appreciably exceed the physiological range; however, there were some changes, as compared to the background data (Table 1). Both cosmonauts revealed shorter atrioventricular conduction time and longer intraventricular conduction during the flight. Thus, the P-Q interval was down to 0.11-0.12 sec (mean of 0.14 sec before the flight) and QRS interval increased to 0.10-1.11 sec (0.07 sec before the flight) in V. I. Sevast'yanov between the 22d and 60th flight days.

No appreciable change was demonstrated in absolute magnitude of electrical systole, or between true and proper levels of this index throughout the examination period (see Table 1).

Starting on the 5th day of the flight, both cosmonauts presented a decrease in amplitude of T waves in the DS lead and mainly in the standard leads. An analogous direction of changes in amplitude of T waves, though to a somewhat lesser degree, was observed in the chest leads, and the T wave in the latter leads was always positive and regular in shape.

In P. I. Klimuk, the amplitude of T waves underwent phasic changes: T_{III} changed from positive to biphasic on the 5th day of the flight, and to negative on the 22d day; by the 46th day of the flight, there was a gradual increase in amplitude of T_{III} almost to the initial level, and on the 53d day it became biphasic again. There was less distinct decrease in amplitude of T_{I,II} and T_{aVF}; during the second half of the flight, the T waves in these leads became stabilized at a somewhat lower level than before the flight. During the breath-holding test in inspiration, P. I. Klimuk presented

moderate decrease in amplitude of $T_{I,II}$ and increase in T_{III} waves; when examined on the 53d day of the flight, the biphasic T_{III} wave during inspiration changed to a positive one (Table 2).

The decrease in amplitude of T waves was relatively less marked in V. I. Sevast'yanov: up to the 37th day, the T wave was positive in standard and chest leads. However, toward the end of the flight, as in the case of P. I. Klimuk, we observed a gradual decline of amplitude of T waves, particularly in the standard III and aVF leads: a biphasic T_{III} was recorded on the 50th and 60th days of the flight, but $T_{I,II}$ and T_{aVF} remained positive, though to a somewhat lesser extent than before the flight. When the EKG was recorded in inspiration, we observed some decrease in amplitude of $T_{I,II}$ waves; on the 31st day, during inspiration, T_{III} increased and became positive, while on the 50th and 60th days it remained biphasic (Table 3).

As a result of the decreased amplitude of T waves, there was a corresponding increase in R/T ratio in standard and chest leads on both cosmonauts. It should be noted that the decrease in amplitude of T waves was not associated with perceptible change in shape of the S-T interval or its position in relation to the isoelectric line. There was some shift to the left of the electrical axis of the heart of both cosmonauts: the α QRS angle decreased from 71° to 60° toward the end of the flight in P. I. Klimuk, and from 86° to 60° in V. I. Sevast'yanov.

During the flight, both cosmonauts endured the physical load on the bicycle ergometer satisfactorily. No clinical manifestations of overfatigue or impaired cardiac activity were demonstrated. With regard to change in pulse rate, the reaction to the test was quite similar to the one observed before the flight. The pulse rate increased on the average from 70-85 to 110-114 per min in P. I. Klimuk and from 60-64 to 96-116/min in V. I. Sevast'yanov. No pathological changes were observed in amplitude and time parameters of the EKG after the load (1-5 min); the shape of the EKG did not undergo appreciable change. However, as compared to the preflight examination, we were able to detect the following distinctions in the reaction to the load: In the first few minutes after they stopped working on the bicycle ergometer, against the background of a faster pulse and corresponding shortening of the R-R interval, both cosmonauts presented an increase in atrioventricular and intraventricular conduction time. Thus, when examined on the 22d day of the flight, in the 1st min after working on the bicycle ergometer, the P-Q interval increased from 0.14 sec (background) to 0.17 sec, QRS increased from 0.06 to 0.10 sec, with decrease in R-R from 0.68 to 0.54 sec in P. I. Klimuk. In V. I. Sevast'yanov, in the 1st minute after the test, the duration of the P-Q interval increased from 0.11 sec (background) to 0.13 sec, with no change in QRS interval and a decrease in R-R interval from 0.98 to 0.83 sec. Before the flight, we observed a less marked change in these indices, mainly in the direction of decrease, in both cosmonauts, in response to the physical load. Furthermore, analysis of the results of the physical load test conducted during the flight revealed that there was a more marked decrease in amplitude of T waves, than in the background, in the response of P. I. Klimuk to the load; examination on the 22d day of the flight after working on the ergometer revealed that the negative T_{III} wave (-0.9 mm) became somewhat more accentuated (-1.3 mm).

Table 1. Changes in conduction indices in P. I. Klimuk and V. I. Sevast'yanov

Cosmonaut	Index	Pre-flight	Days of flight										Postflight days						
			5	14	22	31	37	46	50	53	60	0	1	2	3	7			
P. I. Klimuk	PQ	0,15-0,18	0,12	0,14	0,14	0,15	0,15	0,15		0,14	0,12	0,17	0,16	0,15	0,14	0,17			
	QRS	0,05-0,08	0,09	0,08	0,06	0,10	0,09	0,09		0,09	0,09	0,06	0,06	0,07	0,07	0,06			
	QT	0,34-0,39	0,34	0,34	0,31	0,37	0,35	0,36		0,35	0,39	0,33	0,36	0,37	0,36	0,34			
	RR	0,83-1,05	0,74	0,81	0,68	0,96	0,73	0,80		0,87	0,84	0,74	0,85	0,90	0,84	0,84			
V. I. Sevast'yanov	PQ	0,13-0,15	0,12		0,11	0,15	0,14				0,12	0,13	0,14	0,13	0,13	0,14			
	QRS	0,06-0,08	0,08		0,09	0,10					0,11	0,06	0,08	0,07	0,07	0,06			
	QT	0,33-0,35	0,33		0,38	0,36	0,34				0,36	0,31	0,34	0,34	0,34	0,32			
	RR	0,82-0,96	0,83		0,98	0,86	0,89				0,78	0,64	0,77	0,71	0,72	0,76			

Table 2. Changes in amplitude of T wave, mm, in P. I. Klimuk

Leads	Preflight	Days of flight						Postflight days					
		5	14	22	31	37	46	53	0	1	2	3	7
I	3,0-4,0	2,3	3,8	2,5	2,7	2,0	2,6	2,7	2,5	3,6	3,0	3,0	3,7
II	4,0-5,0	2,4	3,9	2,2	3,4	2,0	3,4	—	3,0	4,5	3,0	4,0	4,0
III	0,5-1,1	±0,6	1,8	-0,9	0,27	0,42	0,85	±0,3	0,5	1,0	0	1,0	0,6
aVR	(-4,0)-(-5,0)	-2,0	-3,1	—	-2,8	-1,8	-2,85	—	-2,25	-3,6	-3,0	-3,5	—
aVL	1,5-2,5	1,3	1,4	—	1,3	1,5	1,13	—	0,6	1,0	1,5	1,0	1,0
aVF	2,1-3,0	1,5	2,8	—	1,5	0,94	1,97	—	1,5	3,0	2,0	2,5	2,5
V ₁	2,3-5,5	2,3	1,4	—	2,8	3,9	3,7	2,9	2,5	3,0	3,0	3,0	2,5
V ₂	6,0-9,0	—	—	—	5,7	—	4,8	—	8,0	9,0	8,5	8,0	8,5
V ₃	7,0-8,5	6,5	—	—	6,5	4,1	4,9	5,5	8,0	8,0	7,0	7,0	8,0
V ₄	7,0-7,6	5,3	—	—	7,5	—	—	—	5,5	5,0	5,5	5,0	6,0
V ₅	5,0-6,5	5,2	—	—	5,5	4,8	—	—	4,0	5,0	4,5	5,0	5,0
V ₆	4,0-5,5	3,7	—	—	4,7	—	—	—	3,0	4,5	3,0	3,5	4,0

Table 3. Changes in amplitude of T wave, mm, in V. I. Sevast'yanov

Lead	Pre-flight	Inflight days					Postflight days				
		5	31	37	50	60	0	1	2	3	7
I	2,0—3,0	1,4	1,95	—	2,1	2,2	2,5	3,0	2,5	3,0	3,5
II	3,0—4,3	2,1	2,1	0,8	2,4	2,2	2,0	3,0	2,5	2,5	3,0
III	1,0—2,2	1,3	0,5	0,4	±0,7	±0,4	1,0	0,5	0,5	0	0,5
aVR	—2,5)— (—3)	—1,6	—1,6	—1,5	—2,1	—2,3	—2,0	—3,0	—2,0	—3,0	—3,5
aVL	1,0—1,6	0,6	1,3	1,0	1,2	1,2	1,1	1,5	0,5	1,5	2,0
aVF	2,0—2,5	1,5	1,0	0,8	1,3	1,1	1,3	1,0	1,0	0,9	1,5

Thus, the clinical and electrocardiographic examination of P. I. Klimuk and V. I. Sevast'yanov failed to demonstrate deviations that exceeded appreciably the physiological range. The functional state of the myocardium remained on a rather high level throughout the flight, and the noted changes did not restrict the cosmonauts' work. The demonstrated changes in time and amplitude parameters of the EKG were not pathological; they disappeared soon after the return to earth, and they were due primarily to adaptation of the cosmonauts' body to weightlessness and other space flight factors. In our opinion, of the changes observed, the change in conduction function of both cosmonauts merits particular attention.

The genesis of the changes detected on the EKG is complex and for the time being it is not completely clear. It may be assumed that positional changes, reorganization of extracardiac regulation, water and electrolyte metabolism as well as of systemic and intracardiac hemodynamics, play the chief role in development of these changes. For a number of reasons, including the lack of clearcut correlation between the change in amplitude of T waves and positional changes, it is not deemed possible to completely rule out the possible influence of metabolic changes on the EKG. This question, as well as determination of the prognostic significance of the disturbances observed, require further, purposeful investigation.

The problem of effects of weightlessness on function of the human heart is gaining particular urgency, since the duration of flights, the work load of cosmonauts and their age are constantly increasing.

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CHANGES IN HEMODYNAMICS AND PHASIC STRUCTURE OF THE CARDIAC CYCLE IN THE CREW ON THE SECOND EXPEDITION OF SALYUT-4

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[Article by V. G. Doroshev, T. V. Batenchuk-Tusko, N. A. Lapshina, Yu. A. Kukushkin, N. D. Kalmykova and V. N. Ragozin, submitted 2 Mar 76]

[Text] The measured physical exercise test is among the traditional practices in clinical medicine and athletics. First used on the Voskhod spacecraft [1], it was then used during virtually all of the Soviet [2, 3, 4] and American [13] manned flights.

It became apparent, from the results of such studies, that there are two main problems under weightless conditions: difficulty in measuring the load generated by stretching expanders, and difficulty of performing complex examinations, since active movements hinder proper recording of physiological indices. Analysis of the results of these studies revealed that most indices did not differ appreciably from preflight levels, while the postflight examinations revealed an overt decrease in tolerance of the same loads [7, 8, 11].

In preparing for the flight of the Salyut-4 orbital research station, a bicycle ergometer was installed on board for the purpose of functional tests with a physical load, and this made it much simpler to create standard testing conditions. We used the same equipment as on the Salyut and Salyut-3 orbital stations to record the circulatory parameters.

Method

The test involving a physical load was conducted using an analogue of the onboard bicycle ergometer in the preflight and postflight periods. On the ground, the cosmonaut mounted the bicycle ergometer lying at a 10° angle from the horizontal line, holding on to the frame handles. In flight, he strapped himself to the frame and pedaled, holding on to the handles.

In all cases, exercise time had to constitute 5 min at the rate of 450 kg-m/min and pedaling rate of 60 r/min. Thus, overall exercise in 5 min constituted 2250 kg-m/min, i.e., it was moderate.

The physiological parameters were recorded in the initial position, 2-3 min before pedaling. The equipment was left on throughout the test. Recording was continued for 2-5 min of the recovery period. It was possible to obtain good tracings starting in the first 5-10 sec after stopping the exercise.

In analyzing the dynamics of the obtained data, the average values of indices recorded before the test were taken as the background.

Results and Discussion

During the flight on the Salyut-4 orbital station, the commander performed the physical load test and recorded parameters on the Polinom unit three times, and the flight engineer, five times. The crew members did not experience any subjective discomfort. The exercise performed by the cosmonauts constituted 2100-2200 kg-m/m in 5 min at the pedaling rate of 56-60 r/min.

On the 46th day, both crew members of the Salyut-4 orbital research station underwent comprehensive examination of circulation, during performance of the exercise, with recording of arterial pressure, stroke and minute volume and vascular tonus indices.

The inflight reaction of P. I. Klimuk, with regard to arterial pressure response to the physical load was close to the preflight one, although the absolute pressure figures were higher. The only exception was diastolic pressure: on earth, it increased after pedaling and in space, it decreased. The pulse pressure increment constituted 25% in flight and 17% on earth. The dynamics of rate of distribution of pulse wave over elastic arteries were close to the findings on the ground. In flight, the minute volume of blood increased by only 12%, while the preflight increase reached 35%. Systolic blood volume decreased similarly to the preflight extent. The mean dynamic, pulse pressure and rate of distribution of the pulse wave were still high in the 2d-3d min of the recovery period.

Absolute arterial pressure levels were also higher than preflight levels in V. I. Sevast'yanov. The percentile increment of arterial pressure corresponded to figures recorded on the ground. However, pulse pressure was lower than in the preflight period during the 1st min of the recovery period. During the 1st minute of work, systolic blood volume dropped by 30%, and on earth the drop constituted 19%. There was virtually no change in minute blood volume. The rate of distribution of the pulse wave over elastic arteries in the 1st min after pedaling was 8% higher than the preflight level. In the 2d min after work, the heart rate and arterial pressure remained high.

On the 3d day after landing, the functional test with a load of 2250 kg-m in 5 min was tolerated worse than in the preflight and inflight periods; however, it was never interrupted due to worsening of the subjects' condition.

The postflight hemodynamic changes were in the same direction as during the flight, but more marked.

Upon completion of the exercise, the arterial pressure of P. I. Klimuk was higher than preflight and inflight levels. The pulse wave was 41% higher (only 20% higher in the preflight period). Systolic blood volume diminished by one-third and cardiac output decreased by 14%.

In V. I. Sevast'yanov, arterial pressure after the physical load was higher than in the preflight and inflight periods; systolic blood volume decreased by one-third in the 1st min, as was the case in flight. There was a more marked decrease in cardiac output (by 15%), as compared to the inflight level. The rate of distribution of the pulse wave over elastic arteries increased to a lesser extent (by 7%) than in weightlessness.

It is known that the exercise tolerance test is associated with consistent changes in contractile function of the myocardium and parameters of intracardiac hemodynamics [6, 9, 10]. As in previous flights [4], the apical kinetocardiogram was recorded on the Salyut-4 orbital station to examine the heart.

After inflight pedaling on the ergometer, the kinetocardiogram complexes remained essentially the same in shape as before the exercise. There was a 30-40% increase in amplitude of the systolic part of the curve, versus a 20% increment in the preflight period. With reference to dynamics of the main phases of the cardiac cycle, the most marked changes were observed in ejection time. Regardless of duration of flight, it was 13-25% shorter for the first 5-10 s of the recovery period in P. I. Klimuk. At this same time, there was a 10-25% reduction of the phase of isovolumetric contraction in P. I. Klimuk, and 20-25% reduction in V. I. Sevast'yanov. The changes in the phase of isometric contraction were less marked than in the preflight period. As a result, there was relative increase in interphase index, K [5].

The ejection period diminished by 14-26% in the 20th-30th second after the exercise test in P. I. Klimuk, and by 15-27% in V. I. Sevast'yanov. These changes were close to those observed in the preflight period. The isometric contraction phase diminished by 10-17% in the commander, i.e., it was shorter than on earth. In the flight engineer, the reduction was essentially the same as before the flight (10-20%). Coefficient K remained high in P. I. Klimuk, and held at the preflight level in V. I. Sevast'yanov. The ejection and isometric contraction phases remained 10% shorter 1 min after the test in the commander and 20% shorter in the flight engineer. These changes were less marked or the same as before the flight. In the 2d-3d min of the recovery period, the ejection and isometric contraction phases were virtually normalized in P. I. Klimuk, as they were on earth, whereas in V. I. Sevast'yanov the ejection phase remained shorter. Thus, with the functional test involving physical exercise in weightlessness, the changes in phases of the cardiac cycle were moderate, and they were manifested by relatively mild shortening of the isometric contraction phase and a corresponding elevation of interphase coefficient K.

After landing, in P. I. Klimuk, the ejection and isometric contraction phases were 15-20% shorter in the 1st min after the test and recovery occurred only in the 3d min. In V. I. Sevast'yanov, the changes in these indices in the 30th s and 1st min after the test were the same as in flight, but there was no recovery in the 4th min after the test. In the postflight period, we were unable to record the kinetocardiogram immediately after the test. A study of the phasic structure of the cardiac cycle at a later time (30th s for the flight engineer and 1st min for the commander) revealed that there was slower recovery than under weightless conditions.

On the whole, the results of these studies confirmed the fact that, in weightlessness, the reaction of the circulatory system remains at about the pre-flight level. However, it should be borne in mind that, in weightlessness, the actual load was smaller, not only because the cosmonauts often pedaled at a slower rate, but because they did not expend energy to lift a weight, such as the weight of the legs when the test is performed on earth.

In this flight, which lasted 63 days, as in preceding ones [4], we failed to demonstrate a clearcut correlation between reaction to the load and duration of weightlessness. This is a rather important finding, since it allows us to assess favorably the possibility of performance of physical labor by the crew under conditions of prolonged weightlessness.

The lower levels of circulation volume, elevation of arterial pressure and pulse wave distribution in vessels should be considered among the distinctive circulatory reactions to functional tests with a measured physical load in weightlessness. Interestingly enough, these tendencies increased in the postflight period and, after completion of the test on the bicycle ergometer, we even observed some absolute decrease in cardiac output, the decrease in stroke volume being the same as in weightlessness. Arterial pressure was higher than before or during the flight. There was also a more marked increase in rate of distribution of the pulse wave.

In future studies, one should apparently devote more attention to the methods of measuring blood flow and arterial pressure in the course of the exercise test. The data obtained from the examination of V. I. Sevast'yanov indicate that maximum arterial pressure during pedaling reached 170-175 mm Hg on the 46th inflight day and on the 3d postflight day.

Diastolic pressure was higher during the flight (85 mm Hg) and lower after it (75 mm Hg). We were able to tentatively estimate stroke and minute blood volume in the 2d min of the test on the 3d postflight day. There was no change in stroke volume, as compared to the initial level, while minute volume increased by 42%.

Thus, it may be that, in weightlessness, the physical load is not associated with less changes in hemodynamics, and the absolute decrease of minute blood volume in the recovery period is the result of more intensive reorganization of circulation.

The simplest explanation for the observed hemodynamic changes may be a decrease in circulating blood volume in weightlessness and on the 1st day after landing. In weightlessness, the mechanism of circulatory changes in response to the load is the same as on earth, but with a lower volume of circulating blood, with deposition of blood in the internal organs. The additional deposition thereof in the muscles of the limbs has a more appreciable effect on venous return to the heart. And to maintain arterial pressure, stronger sympathetic activation of arterial vessels is required. Upon completion of the exercise, we actually observe excessive activation, and this should be evaluated as a favorable factor, indicative of satisfactory condition of resistive vessels.

The expounded hypothesis of the effect of smaller circulating blood volume in weightlessness on changes in circulatory reaction to a physical load is quite consistent with a number of observations made in flight. After termination of pedaling, emptying of jugular veins was observed in most cases. It is known that a decrease in return of blood to the heart is associated with the distinctive syndrome of longer isometric contraction phase and shorter phase of ejection. As we have shown above, such a phasic syndrome was observed in weightlessness after the functional test, although it was not very marked. We could not detect it after landing.

A serious place is given to the question of myocardial contractile function in the program of medical research on the Salyut-4 station. It is quite obvious that gross disturbances of myocardial contractility did not develop. Otherwise, this would have been reflected in the dynamics of several of the circulatory indices and, in particular, the shape of the apical kinetocardiogram. There would also have been a decrease in amplitude of this curve due to a decrease in force of cardiac contractions. The lack of these signs of impaired myocardial contractility enabled us to relate the above-mentioned phasic syndrome to relative decrease in venous return to the heart after the physical load, due to additional deposition in muscles. On the 3d postflight day, we also failed to demonstrate impairment of contractile function of the myocardium during the test on the bicycle ergometer.

In summing up the results of these studies with a measured physical load, it should be noted that a test with a load constituting a certain percentage of maximum aerobic force, which was done by the American researchers on Skylab, would apparently be more demonstrative. However, when testing the American astronauts, with load levels of 25, 50 and 75% of the maximum aerobic power, there was no demonstration of dynamics of indices that would warrant the assumption of severe worsening of test tolerance in the postflight period. This leads us to conclude that it would be more important to choose informative physiological indices, rather than magnitude of the load. Unquestionably, continued work in this direction is not only of scientific interest, but definite practical value.

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DYNAMICS OF VENOUS CIRCULATION IN COSMONAUTS ON THE SECOND EXPEDITION OF
SALYUT-4

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by Ye. M. Yuganov, V. A. Degtyarev, A. S. Nekhayev, T. V.
Batenchuk-Tusko, Ye. A. Kobzev, V. S. Bednenko and S. V. Ivanova, submitted
2 Mar 76]

[Text] In weightlessness, with disappearance of hydrostatic pressure, the body fluids are redistributed and there is equalization of blood pressure in veins above and below the heart [3, 12]. Increased blood in the upper half of the body is associated with engorgement of jugular veins, sensation of blood rushing to the head, edema of the nasal mucosa and puffiness of the face. Apparently, it is for this reason that most cosmonauts develop the illusion that the body is turned over or bent backward.

It is interesting to note that this most vivid syndrome of the effect of weightlessness had not been predicted in an analysis of the possible changes in the human body during space flights [15]. It is not encountered when weightlessness is simulated by the method of clinostatic hypodynamia with the body in strictly horizontal position [1, 10]. In spite of its obvious importance, investigation of this syndrome is only at its first stage. Pulse fluctuations in the jugular veins and kinetocardiograms of the right heart were recorded on cosmonauts on the Salyut-3 orbital research station. Photography of the crew of the Skylab orbital station, in infrared light, revealed that the veins of the neck and face remained dilated throughout the 3 months of the flight [14, 17].

In this report, we submit the preliminary results of investigation of venous circulation in the crew of the Salyut-4 orbital research station, obtained on the basis of analysis of graphic tracings of jugular vein pulsation. We observed the dynamics of form of pulsograms and venous blood pressure. The duration of phases of the right heart was measured.

Methods

The duration of the flight on the Salyut-4 was 69 days.

We recorded pulse fluctuations of the jugular veins concurrently with the carotid pulse, so that the overall curve was named the venous-arterial pulsogram (VAP).

A porolon-filled rubber capsule, 4×5 cm in size, served as the pulse pickup; it was placed in the middle third of the neck over the projection of the vascular bundle and secured with elastic tape. A piezoceramic sensor was used to transform the mechanical VAP signals. In weightlessness and the preflight period, the time constant of the equipment was 0.1 s and after the flight, 0.5 s.

The VAP was recorded twice in the preflight period: 3 months and 7 days before the launch. In weightlessness, the studies began on the 8th day on P. I. Klimuk and the 13th day on V. I. Sevast'yanov, and they were repeated at intervals of 3 to 14 days. The cosmonauts were examined 3 and 6 hours, and on the 3d day after landing.

Polinom-2 and Mingograf-81 instruments were used to record the preflight and postflight VAP, the paper being fed at the rate of 50 and 100 mm/s, and during telemetry transmission the rate constituted 70 and 80 mm/s.

We isolated and analyzed the following phlebogram elements on the VAP: atriosystolic wave a , diastolic d , collapses x and y [6, 8]. We studied the maximum amplitude indices of a and d waves (as percentage of amplitude of systolic wave c) and ratio of x to y collapses (x/y). Blood pressure in the system of the jugular veins (P) was measured by an indirect method, based on the effect of disappearance of elements of venous pulse on the VAP with passive movement of the subject's body in the frontal plane, both before and after the flight. Before the flight, we also determined the coefficient of single-valued relationship (K) between the obtained index and magnitude of discharge in a vacuum device (P_1), upon reaching which there was complete disappearance of elements of venous pulse on the VAP. And $K = P/P_1$. The pressure index (P') was calculated from the value of discharge (P'_1) determined in weightlessness, and it constituted $P' = K \cdot P'_1$. By analogy to the classical jugular phlebogram, we measured the phases of the right heart [6, 8]. We estimated pressure in the pulmonary artery according to the nomogram proposed by Burstin [2].

On the 53d day of flight, we measured all of the above-mentioned indices in both cosmonauts against the background of a water and sodium load. We are not submitting these data here, since they will be reported separately.

Results and Discussion

The results of the studies conducted by the crew of the Salyut-4 orbital research station confirmed the fact that there are appreciable changes in venous circulation under weightless conditions. It must be borne in mind

that the studies began only on the 8th day, when there was already considerable regression of signs typical of the very first period of adaptation to weightlessness.

On the 8th-13th day, the VAP of P. I. Klimuk and V. I. Sevast'yanov (see Table) showed an increase in amplitude of *a* and *d* waves, and *x/y* ratio, due to decreased diastolic collapse of *y* (Figures 1 and 2). Usually, such changes in venous components of the VAP are observed with increased filling of jugular veins [4, 5, 9]. This is also indicated by the data obtained from measuring the crew's venous pressure. For the 1st inflight month, jugular blood pressure was 50.0-66.6% higher than the preflight levels. On the 43d-44th inflight day, P. I. Klimuk presented the lowest amplitude indices on the VAP in weightlessness, while the VAP of V. I. Sevast'yanov showed no venous components at all, and the curve had the shape of a sphygmogram of the carotid artery, which could be evaluated as an indication of decreased filling of the jugular veins [11, 16]. At this same time, there was also a drop of venous pressure, which was more marked in V. I. Sevast'yanov.

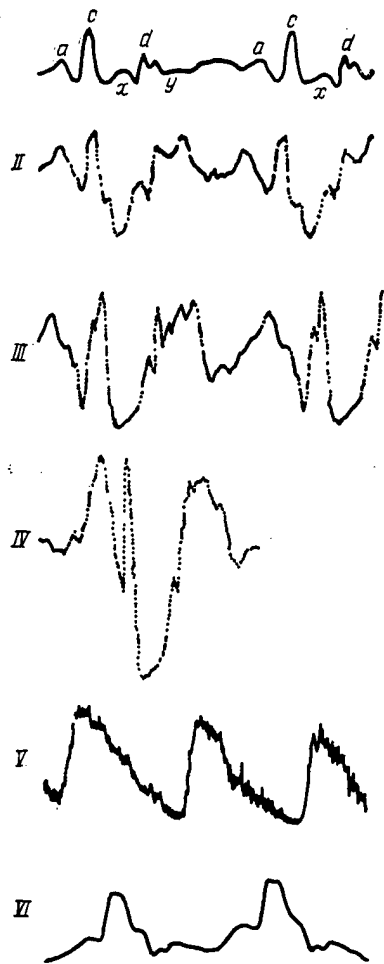


Figure 1.

Dynamics of shape of VAP of P. I. Klimuk in weightlessness, preflight and post-flight periods

- I) preflight
- II, III and IV) 11th, 44th and 53d inflight days
- V) day of landing
- VI) 3d postflight day

Following key applies to this and Figures 2 and 3:

- a*) atriosystolic wave
- c*) systolic wave
- d*) diastolic wave
- x*) systolic collapse
- y*) diastolic collapse

Index	P. I. Klimuk						V. I. Sevast'yanov								
	flight			inflight			pre-flight			inflight					
	7	8	11	29	44	60	0	3	7	13	27	43	55	0	3
HR	60	68	76	65	70	67	80	68	65	80	60	—	—	84	78
A _a	46	100	86	81	86	79	×	28	68	87	52	—	—	×	×
H _d	60	84	100	95	89	87	—	28	45	94	68	—	—	—	—
P	1,25	3,30	2,23	1,40	1,50	1,90	—	0,80	1,37	2,30	1,48	—	—	—	—
SSA	2,1	—	3,5*	3,5**	1,4	1,4	0	2,1	4,0	6,0**	6,0	0	0	0	0
T	0,08	0,06	0,06	0,06	0,06	0,06	—	0,06	0,09	0,06	0,07	—	—	—	—
E	0,09	0,12	0,11	0,10	0,09	0,07	—	0,08	0,09	0,11	0,12	—	—	—	—
IR	0,290	0,279	0,250	0,272	0,262	0,279	—	0,280	0,300	0,264	0,310	—	—	—	—
P _{Pa}	0,07	0,06	0,06	0,07	0,07	0,07	—	0,07	0,06	0,06	0,07	—	—	—	—
	20	25	25	25	30	25	—	30	15	30	20	—	—	—	—

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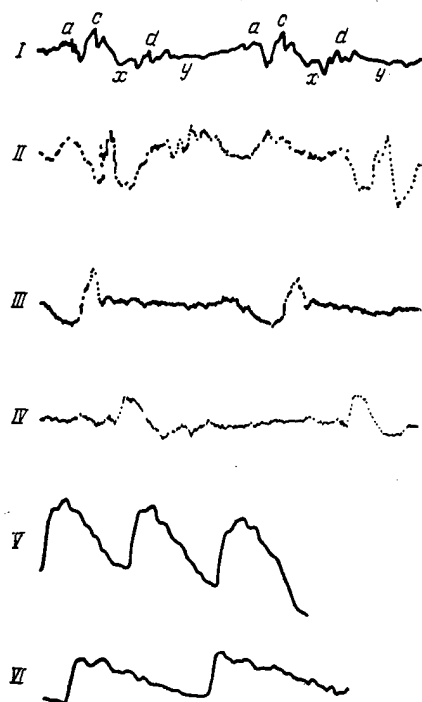


Figure 2.
Dynamics of form of VAP of V. I.
Sevast'yanov in weightlessness, preflight
and postflight periods

- I) preflight
- II, III, IV) 13th, 43d and 53d inflight
days
- V) landing day
- VI) 3d postflight day

The greatest differences of phase indices, as compared to preflight ones, were observed on the 8th and 11th days in P. I. Klimuk. Thus, on the 11th day there was 25% shortening of atrial systole and 13.8% decrease in ejection, while isometric relaxation decreased by 14.3%. The contraction [tension] period increased by 22.2%. The duration of the atrial systole remained unchanged on the 29th, 44th and 60th days, while the other indices showed a tendency toward moving to the preflight values.

Tests made on V. I. Sevast'yanov on the 13th and 27th days showed more marked changes in duration of periods, and the periods of contraction and isometric relaxation became longer, while the other indices differed little from preflight levels on the 27th day.

In our opinion, these phase dynamics warrant the assumption that there was no marked overload on the right heart under weightless conditions.

As we see from the Table, in P. I. Klimuk, blood pressure in the pulmonary artery at rest rose by no more than 25% up to the 60th inflight day; in V. I. Sevast'yanov, it rose by 100% on the 13th day and dropped on the 27th day to 33.3% above the preflight index.

Evidently, elevation of pressure in the pulmonary artery during the 1st month of flight could be interpreted as an adaptive reaction of the pulmonary circulation (increased resistance in pulmonary arterioles as a result of

decrease in their lumen) directed toward averting an overload on the left atrium. It is difficult to interpret the absence of dynamics in this index in the 2d inflight month in P. I. Klimuk.

There was poor correlation between changes in jugular filling and pressure, and subjective indices. Thus, in spite of elevated pressure in the jugular veins for the 1st inflight month, P. I. Klimuk did not experience the sensation of blood rushing to the head, or else it was minimal. Conversely, V. I. Sevast'yanov had a distinct such feeling. Interestingly enough, even after significant drop of venous pressure, V. I. Sevast'yanov continued to feel a rush of blood to the head, although he evaluated its intensity at 15, 10 and 5% of the sensation observed in the acute period of adaptation, at different stages of the flight. It is interesting that both cosmonauts noticed reappearance of natural lines on the face after 1-1.5 months, which had become smooth previously due to facial edema at the early stage of the flight. This served as an indirect confirmation of the signs of decreased filling of vessels of the head and, perhaps, not only the vessels, but extravascular tissular fluid.

Evidently, the demonstrated inconsistency between subjective and objective data may be attributed to both individual differences in proprioceptive sensitivity and differences in functional capabilities of collaterals that remove blood from the pool of the internal jugular vein. We do not have a concrete answer to this question.

Nor can we fail to call attention to some discrepancy between the results of examination of venous circulation in weightlessness, which we performed, and the data of American authors who had the impression that the veins of the neck and head remained dilated throughout the 3 months of flight in crew members of the third expedition on the Skylab station [14].

Central venous pressure (CVP) in weightlessness was first measured on the monkey, Bonny, during the 9-day orbital flight on Biosatellite-III in 1969 [18]. This was done by the method of catheterization of the right atrium and inferior vena cava, i.e., a direct method. In the first 5 days of flight, the CVP almost doubled, as compared to the preflight level, and from the 6th day on it progressively dropped to the 7th-8th day. However, we cannot be certain enough that the drop of venous pressure is a normal adaptation response to weightlessness, in view of the fact that the animal's condition worsened severely on the 8th-9th day, and the monkey died after landing.

Among the possible mechanisms of diminished jugular filling and venous pressure in the crew of Salyut-4, in our opinion, the most obvious ones are deposition and redistribution of blood from the central regions into the internal organs, and first of all the liver and spleen.

There can apparently be loss of plasma in weightlessness too, and it could also be the cause of venous pressure drop. According to the data of Echt et al. [13], a 500 ml decrease in blood volume is sufficient for a 30-40% CVP drop.

On the basis of these data and the results of our investigations, it can be assumed that the 33.4-100% pressure drop, as compared to preflight levels, observed in the cosmonauts in the 2d month of the flight may be due to elimination of up to 500-1200 ml blood from active circulation.

However, this assumption has not yet been adequately confirmed and requires further investigation.

We conducted a series of experiments, involving the use of pressure cuffs (100 mm Hg) on the upper third of the thighs of 24 volunteer subjects, in order to investigate the effect of deposition of blood on jugular filling and blood pressure. In all instances, the amplitude indices of the phlebographic elements of the VAP and venous pressure in the jugular veins diminished in the 4th-5th min after applying pressure. Solti and Iskum [19] obtained analogous results. The findings made on VAP recordings of P. I. Klimuk, on the 11th, 20th and 48th inflight days also speak in favor of the foregoing. The VAP was completely formed like a sphygmogram (SPG) of the carotid artery in the 1st minute after the bicycle ergometer test (Figure 3). The venous components appeared in the 2d-3d min. Evidently, decreased filling of cervical veins after the physical exercise in weightlessness occurred as a result of redistribution of blood in the veins of the lower extremities [14]. This is a very important finding, since it shows the effectiveness of using the physical exercise in weightlessness to prevent redistribution of blood in the upper parts of the body.

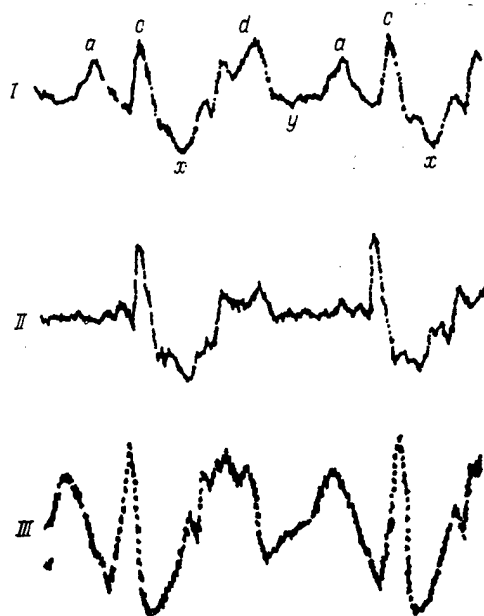


Figure 3.
Dynamics of form of VAP of P. I. Klimuk
on 11th inflight day during functional
test on bicycle ergometer

I) at rest, before the test
II and III) 1st and 3d min, respectively,
after stopping pedaling

There was no pulsation in the jugular veins of both cosmonauts in horizontal position, and only the carotid SPG was recorded in the postflight period, 3 and 6 h after landing. We obtained analogous results following short flights, as well as when we examined the crews of Salyut-3 orbital research station and the first crew of the Salyut-4 station. The decrease in

filling of jugular veins and drop of pressure therein after landing are apparently due to additional redistribution of blood under the influence of earth's gravity. Return of venous pressure to the preflight level occurred on the 3d day in P. I. Klimuk and corresponded to restoration of initial orthostatic stability. There was no appearance of venous components on the VAP of V. I. Sevast'yanov at this time.

Thus, the changes in venous circulation in weightlessness are more obvious and persist for a longer time than changes in other hemodynamic indices.

There were some changes in venous circulation in weightlessness. During the 1st month of the flight, blood pressure and filling of jugular veins increased, while these indices dropped below preflight levels in the 2d month. The drop of venous pressure to preflight or lower levels by the end of the 1st or start of 2d inflight month should apparently be evaluated as a sign of adaptation of the organism. At this time, we can already refer to a new level of homeostasis and completion of the main adaptational reactions that were typical in the acute (up to 3-4 days) and subacute (to the 7th-12th day) periods, as well as subsequent period of relative stabilization of physiological indices. We attributed the pressure drop in the jugular veins, observed from the 2d month of flight on, to deposition of blood and redistribution thereof in abdominal organs. If this hypothesis is corroborated, several new problems will arise, with regard to evaluating the condition of cosmonauts in the course of long flights and necessity of developing preventive measures against the deleterious effects. One of the most important directions of future research will be, in particular, the study of the effects of redistribution of blood on the function of the liver and other organs, and possible sequelae of prolonged deposition of blood in them.

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EVALUATION OF PULSE RATE DYNAMICS IN MEMBERS OF THE SECOND CREW OF SALYUT-4
AT REST AND DURING INFLIGHT PERFORMANCE OF FUNCTIONAL TESTS

Moscow KOSMICHESKAYA BIOLOGIYA IN AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 37-42

[Article by O. G. Itsekhovskiy, A. P. Polyakova and V. R. Lyamin, submitted
19 Mar 76]

[Text] Manned space flights have shown that evaluation of changes in heart
rhythm is one of the most informative means of determining the nature of
adaptation of the cardiovascular system to weightlessness [1, 2, 3, 4].

For this reason, during the flight on the Salyut-4 orbital station, we
studied the pulse rate response of cosmonauts P. I. Klimuk and V. I.
Sevast'yanov, both at rest and during functional tests with LBNP (lower
body negative pressure) and physical exercise on a bicycle ergometer.
American specialists conducted analogous studies during the flight of the
Skylab orbital station.

Methods

During the flight on the Salyut-4 station, 11 functional tests were made on
the bicycle ergometer with each crew member (8th, 11th, 14th, 22d, 29th, 36th,
37th, 46th, 48th, 53d and 57th days on P. I. Klimuk; 13th, 14th, 21st, 22d,
25th, 35th, 37th, 45th, 46th, 53d and 55th inflight days on V. I. Sevast'yanov)
and 9 LBNP tests (14th, 18th, 22d, 28th, 31st, 37th, 44th, 53d and 60th days
on P. I. Klimuk; 10th, 14th, 22d, 27th, 31st, 37th, 43d, 53d and 60th days
on V. I. Sevast'yanov). In addition, the physiological parameters at rest
were recorded on each cosmonaut once every 2-3 days.

The LBNP test was performed using the Chibis kit [suit?] in decompression
mode: -25 mm Hg for 2 min and -35 mm Hg for 3 min. We observed the recovery
period for 5 min. In order to evaluate pulse dynamics during physical
exercise on the ergometer, we determined the time at which the rhythm became
stable, absolute and relative values (percentage of initial value), and
time of rhythm stabilization after the load. In each test, we estimated
the actual physical load in kilogram-meters/min according to pedaling rate.
The indices were recorded before the test, 5 min during the load and 5 min

after. In this test, the load had to constitute 440 kg-m/min with a pedaling rate of 60 r/min. The pulse rate was counted primarily on the EKG. The obtained data were submitted to statistical processing on an electronic computer.

Results and Discussion

Before the launch, there was a gradual increase in the cosmonauts' pulse rate. During the orbit insertion period, it increased by 40/min in P. I. Klimuk and 37/min in V. I. Sevast'yanov (at the time of the clinicophysiological examination, the pulse of P. I. Klimuk was 71/min and that of V. I. Sevast'yanov, 73/min). After orbit insertion, the mean daily pulse rate of both cosmonauts presented a marked tendency toward decreasing. However, it was higher, with statistical significance, than the background rate for the first few days of flight in P. I. Klimuk. Thereafter, the changes were in the range of fluctuations in the background examination, with the exception of the 28th day, when the heart rate of the spacecraft commander had increased to 95/min. As the spacecraft entered in orbit, the lowering of pulse rate of V. I. Sevast'yanov was more marked. This index reached the preflight level on the 1st-2d day of the flight, showing a tendency toward further decline. However, this decline in relation to the background was statistically reliable only on the 13th, 14th, 25th and 27th days. On the 63d inflight day, during the last 2 passes of the orbit, before the descent, the pulse rate of both crew members increased again (to 94/min in P. I. Klimuk and 100/min in V. I. Sevast'yanov) (Figure 1).

In both cosmonauts, there was a consistent increase in pulse rate in all LBNP tests. With rarefaction of -35 mm Hg, the heart rate 8 days prior to the flight increased to about the same extent in P. I. Klimuk and V. I. Sevast'yanov (by 35 and 31%, respectively). Upon completion of the test, the spacecraft commander's pulse remained above the initial levels for 5 min, whereas recovery occurred in the 1st min after removal of pressure in the flight engineer.

In spite of the general tendency toward a slower heart rate during the flight, which was observed at rest, the pulse rate recorded before and after the tests with LBNP was higher in most cases, in both cosmonauts, than in preflight tests (Figure 2). The initial pulse rate was particularly high in P. I. Klimuk on the 18th and 29th days, and with the LBNP test, on the 14th, 28th and 31st days. In V. I. Sevast'yanov, the changes in heart rate were less marked, in comparison to the preflight period; however, the pulse rate was highest on the 43d inflight day, both before and during the test. With reference to pulse rate dynamics during rarefaction, as related to initial figures, it can be noted that, on the 14th inflight day, P. I. Klimuk presented the most marked response, for the entire flight period, of heart rhythm to rarefaction, when the pulse rate increased by 50%. Conversely, in tests made on the 18th and 28th days, the reaction was mild. In these cases, the increase in pulse rate during the LBNP test occurred after a high initial level (85-96/min), and it only constituted 6-8%. In the tests on the 22d, 31st, 37th, 44th, 53d and 60th days, the pulse increment in

response to decompression was in the range of 20-33%, while the initial pulse rate was about the same (71-76/min). Thus, we observed a more severe response, as compared to the preflight test, of heart rhythm on the 14th inflight day, in the test with LBNP on P. I. Klimuk. In the other inflight tests it was less marked.

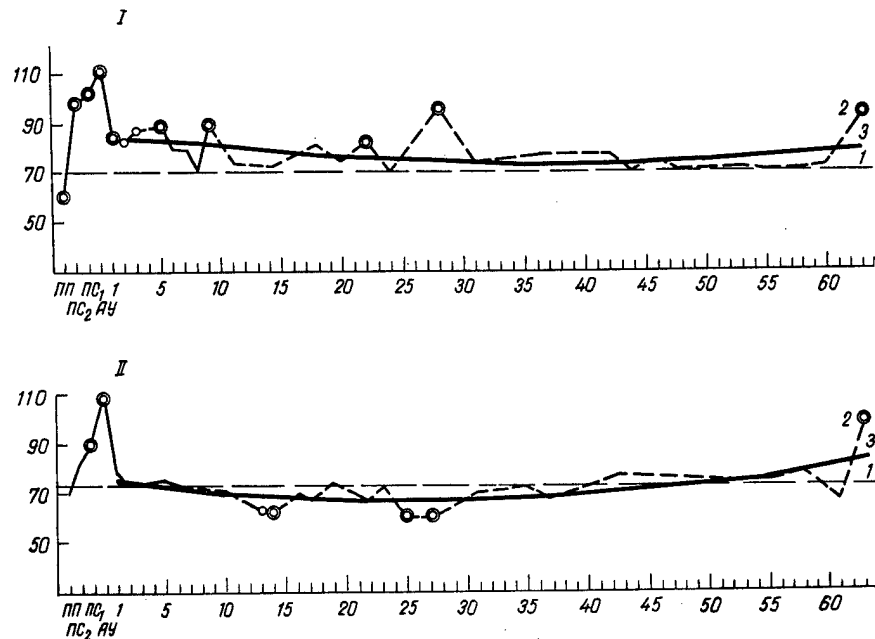


Figure 1. Dynamics of mean heart rate of P. I. Klimuk (I) and V. I. Sevast'yanov (II) at rest, during orbital flight; x-axes, days of orbital flight; y-axes, cardiac contractions per minute

- 1) preflight
- 2) various inflight periods (circles refer to values statistically different from preflight data)
- 3) smoothed results of actual data
- II II) preflight period (9 days before launch)
- II C₂) 60-min countdown ["1-hour readiness"]
- C₁) 5-min countdown
- AY) powered flight

In V. I. Sevast'yanov, in almost all of the inflight tests with LBNP, the changes in pulse rate, as compared to initial levels, were also less marked than in the preflight test. The maximum increase constituted 19-36%, and in the test made on the 14th day it did not even exceed 10%. The only exception was a somewhat more pronounced reaction to decompression with reference to heart rhythm in the test on the 43d day of the flight, when

it increased by 36%. As a rule, recovery of original rhythm after LBNP occurred in the 1st-2d min in both cosmonauts.

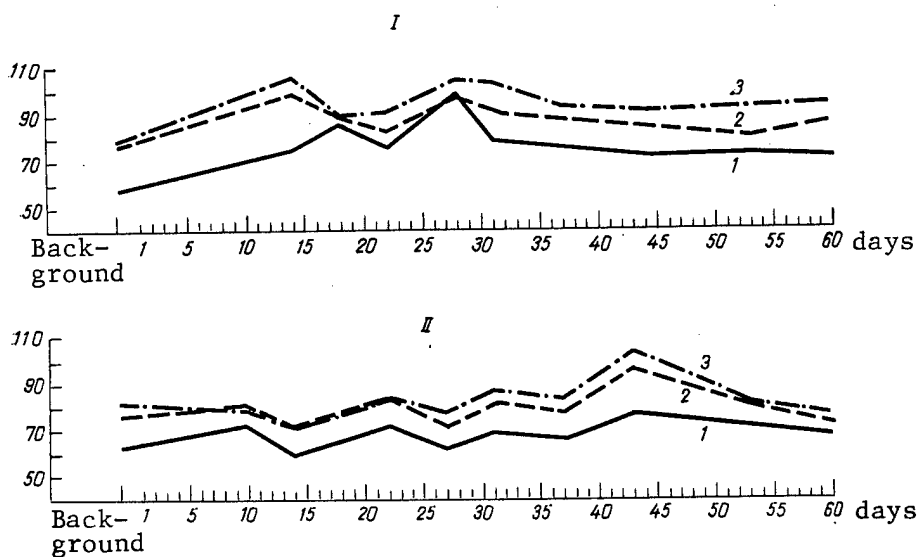


Figure 2. Dynamics of heart rate of P. I. Klimuk (I) and V. I. Sevast'yanov (II) during inflight functional test with LBNP

- 1) mean levels before test
2 and 3) maximum levels with pressure of -25 and -35 mm Hg, respectively

In the bicycle ergometer test performed on P. I. Klimuk before the flight, we observed an increase of 85% in pulse rate by the 3d min of the physical load (from 68 to 126/min) with stabilization in the 2d min of pedaling. In the preflight test on V. I. Sevast'yanov, the pulse rate showed a 67% increase (from 66 to 110/min) by the 3d minute of pedaling, and the rhythm became relatively stable after 1^m40^s. During the recovery period, the former cosmonaut had a pulse rate of 20 more per min than the initial level for 5 min, whereas in the latter, stabilization of rhythm was observed in the 2d min and complete restoration, in the 4th min. In the inflight tests, the maximum pulse rate during exercise did not exceed 130/min for P. I. Klimuk and 116/min for V. I. Sevast'yanov; as a rule, tachycardia induced by the load was less marked in the flight engineer than the spacecraft commander. It must be mentioned that the pedaling force did not correspond to the planned level (440 kg-m/min) in some of the inflight tests. Thus, it was greater than planned (mean of 474 kg-m/min) in the test on P. I. Klimov on the 11th day and, on the contrary, smaller on the 29th, 36th and 37th days (382, 385 and 404 kg-m/min, respectively). In V. I. Sevast'yanov, the exercise tests involved a lower force on the 22d, 25th, 35th and 37th days (average of 381-409 kg-m/min), and a higher one on the 21st day (480 kg-m/min). In each test, the velocity of pedaling was not always uniform: it was higher at the start of the test, then gradually declined.

In assessing the pulse reaction to physical exercise during inflight tests, we can mention some variation of heart rhythm dynamics. In the first 4 tests on P. I. Klimuk (8th, 11th, 14th and 22d days) there was a distinct tendency toward lower pulse reaction to the physical load. Thus, on the 8th inflight day, after the test, he presented rapid stabilization of rhythm and complete recovery in the 3d-4th min, which was not observed in the preflight test. On the 11th day, in spite of higher functional load, the pulse response was the same as in the preflight period. In the test made on the 14th inflight day, in the 1st min of exercise at the rate of 498 kg-m/min, there was only a 38% increase in pulse rate, whereas in previous tests this index constituted 44% with a lower load. The exercise test made on the cosmonauts on the 22d day of flight was associated with the lowest response. Even in the 1st min, when force of pedaling reached 505 kg-m/min, the pulse rate increased by only 23%. The maximum increase occurred in the 3d min, and it constituted 36%. The recovery period was associated with a negative phase of pulse rate. It must be noted that, at this stage of the flight, the tests with LBNP on this cosmonaut were also associated with a moderate response of cardiac rhythm. In tests made halfway into the flight, on the 29th, 36th and 37th days, the force of pedaling decreased, so that there was also a decrease in severity of tachycardia. In these tests, maximum pulse rate was in the range of 103-118/min, and the increase constituted 39-56% of the initial level.

The pulse response to the physical load was about the same in tests made on the 46th, 48th and 53d inflight days. In these tests, maximum pulse increment constituted 60-61% (from 71-75 to 110-118/min). The pedaling force constituted a mean of 446, 437 and 419 kg-m/min. Time of stabilization of the rate also differed: 1^m20^s on the 46th day, 2^m10^s on the 48th and 50 s on the 53d. At the same time, recovery of the rate to the initial level occurred in approximately the 3d min after pedaling in all 3 tests.

The increase in pulse rate during the functional test corresponded to the preflight level in the first two inflight tests on V. I. Sevast'yanov (13th and 14th days), in spite of some decrease in pedaling force. The duration of transitional processes in dynamics of pulse rate, during and after the test, diminished somewhat, while restoration of background rhythm (on the 13th day) was demonstrated in the 3d min after the test.

The test made on the 21st inflight day involved stronger energy than planned (480 kg-m/min). However, in this test, as was the case in P. I. Klimuk in the test made on the 22d day, the pulse rate increment recorded in the 1st, 2d and 3d min did not exceed 36%. Thus, both cosmonauts presented a less marked pulse response to the physical load during this period. In the tests made on the 22d, 25th and 32d days, along with decrease in load, there was also a decrease in pulse response. The relationship between pulse rate increment and pedaling force was also indicative of a diminished response referable to cardiac rhythm to the load, as compared to preflight data. In the next tests, made during the second half of the flight (45th, 46th, 53d and 55th days), the pulse rate increased by 43-57%, reaching 116/min, which was negligibly higher than the preflight response (110/min). Thus, the

cardiac rhythm response to a measured load was close to the preflight level during the inflight period, in V. I. Sevast'yanov, and in some cases it was even less marked.

The above data are indicative of rather adequate tolerance of physical exercise tests by both cosmonauts during the flight. The changes in pulse rate did not exceed the adopted norms. In evaluating the reaction of the cosmonaut's heart rate to a measured load, we can merely mention some variations of dynamics of cardiac rhythm within the normal range.

Analysis of the pulse response to the physical load as a whole, according to all tests, revealed that adaptation of the body to physical work in weightlessness was greater in P. I. Klimuk than before the flight. The only exception was the test made on the 29th inflight day, which involved the lowest pedaling force. The latter was, perhaps, due to some decrease in overall efficiency of the cosmonaut.

The inflight pulse rate responses of V. I. Sevast'yanov were somewhat less marked or the same as in preflight tests. A decreased response of heart rate to the physical load was observed in both cosmonauts, in tests made on the 21st and 22d inflight days. At this same time, V. I. Sevast'yanov pedaled with greater force. It may be assumed that the efficiency of both cosmonauts improved at this time, and it was associated with a sympatho-tonic background in the rhythm of cardiac contractions.

Thus, the dynamics of pulse rate at rest and during functional tests with LBNP and on a bicycle ergometer failed to demonstrate appreciable differences in either cosmonaut, as compared to preflight data. This was generally indicative of good adaptation of the crew to a long orbital flight and readiness of regulatory mechanisms of the cardiovascular system to the impending return to earth.

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PREDICTION AND ANALYSIS OF COSMONAUTS' PULSE RATE BY THE METHOD OF
EXTRAPOLATION MODELING IN THE CLASS OF DIFFERENTIAL EQUATIONS

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[Article by V. K. Vasil'yev, A. A. Guyev, A. B. Savvin and Yu. M. Svirezhev,
submitted 30 May 75]

[Text] Let us consider a simplified scheme of the effects of space flight
factors on the cardiovascular system (CVS) of cosmonauts:

$$\frac{u(t)}{\text{reduced to input disturbance}} \rightarrow \text{CVS} \rightarrow \frac{x(t)}{\text{pulse rate}},$$

where $x(t)$ is pulse rate (PR) as a dynamic process occurring in current
time (days) and $u(t)$ is the overall effect of all factors inherent in
space flight reduced to CVS input.

If we construe $u(t)$ to refer to the constant factors determined expressly
by space flight (weightlessness, psychological load, etc.) that are not
inherent in "ground" conditions, the effects of the space environment could
be arbitrarily described by a function, such as:

$$u(t) = \begin{cases} 0 & \text{--preflight} \\ 1 & \text{--inflight} \\ 0 & \text{--postflight} \end{cases} \quad (1)$$

According to the methodology of theory of automatic regulation, the CVS can
be viewed as a complex dynamic system, the processes of which are entirely
determined by the structure and parameters of the system, factors to which
it is exposed and initial state of the system to itself. The complexity
and, mainly, lack of full description of CVS regulatory processes during
space flights compel us to search for some generalized indirect parameters
that would approximate, at least roughly, but accurately the processes of
CVS adaptation to flight conditions. One possible method of such evaluation
of CVS regulation is identification thereof in some classes of dynamic
models, on the basis of inflight data on pulse rate. If we consider that
the models are in the class of linear differential equations:

$$\sum_{i=0}^n a_i x^{(i)}(t) = \sum_{i=0}^m b_i u^{(i)}(t), \quad (2)$$

then, by defining the model for each day of flight, as new data are received, it can be used to forecast the PR several days ahead. For this, it is enough to solve the equation obtained with t equaling the predicted days, and the initial conditions are determined by derivatives of $x(t)$ on the eve of issuing the forecast of these PR.

The optimum structure of the model (i.e., setting n and m) can be selected on the basis of "running through" the forecast on the available data on PR changes in cosmonauts involved in previous flights, on the condition of minimal forecast error. Such a "run-through" was made with reference to the flight data of the Soyuz-9 spacecraft. As a result, model (2) was chosen the following form:

$$x(t) + a_1 \dot{x}(t) + a_2 \ddot{x}(t) = b_0 u(t), \quad (3)$$

where a_1 , a_2 and b_0 are parameters determined by the method of analytical differentiation [1]. The new PR data, as received daily, are used to define the parameters of equation (3) which, for this reason, we shall call "current."

From equation (3) we can find time constant T and extinction decrement ξ :

$$T = \sqrt{a_2}; \quad \xi = a_1/2\sqrt{a_2}, \quad (4)$$

on the basis of which conclusions can be derived about the quality of CVS regulation in each cosmonaut. Time of cosmonauts' adaptation to flight conditions can be judged according to:

$$t_p \approx \frac{3}{|\operatorname{Re} s_i|}, \quad (5)$$

where the denominator is the modulus of real roots of the performance [characteristic] equation:

$$a_2 s^2 + a_1 s + 1 = 0.$$

The period of damped oscillations is of interest to analysis of changes in PR indices:

$$\Omega = \frac{2\pi T}{\sqrt{1-\xi^2}}, \quad (6)$$

which characterizes the rhythm of CVS function, as determined by the specific factors of space flight.

Using the method described and current differential equations (let us arbitrarily call them type 1 models), we forecast the PR for 1 day, and in some cases for 2 and 3 days for cosmonauts who were members of the Soviet crews of Salyut-1 (cosmonauts No 1, No 2 and No 3) and Salyut-4 (first expedition, cosmonauts No 4 and No 5) spacecraft, and we "ran through" the forecast of PR of cosmonauts on the American spacecraft, Skylab-3 (cosmonauts Nos 6, 7, 8).

Unfortunately, we must mention that we did not have data on the PR of the American astronauts for the first 5 days, which added some uncertainty and doubts to the comparative analysis of the results on all cosmonauts illustrated in Figures 1-3.

Upon completion of the space flights, we determined the individual equation for each cosmonaut, averaged out according to all current differential equations (3) obtained in flight. These equations (type 2 models) were as follows:

Cosmonaut № 1:	$x(t) + 2,04$	$\dot{x}(t) + 4,9$	$\ddot{x}(t) = 77,7$
» » 2:	$x(t) + 2,35$	$\dot{x}(t) + 2,8$	$\ddot{x}(t) = 61,2$
» » 3:	$x(t) + 1,78$	$\dot{x}(t) + 2,2$	$\ddot{x}(t) = 66,3$
» » 4:	$x(t) + 1,11$	$\dot{x}(t) + 1,0$	$\ddot{x}(t) = 66,9$
» » 5:	$x(t) + 0,38$	$\dot{x}(t) + 1,2$	$\ddot{x}(t) = 70,4$
» » 6:	$x(t) + 2,05$	$\dot{x}(t) + 16,69$	$\ddot{x}(t) = 67,9$
» » 7:	$x(t) + 0,63$	$\dot{x}(t) + 1,98$	$\ddot{x}(t) = 67,9$
» » 8:	$x(t) + 0,57$	$\dot{x}(t) + 4,98$	$\ddot{x}(t) = 53,5$

(7)

These equations were then used to calculate the parameters characterizing CVS function in each cosmonaut.

In addition, we determined the equation (type 3 model) that was the mean for the first three cosmonauts:

$$x(t) + 2,1\dot{x}(t) + 3,2\ddot{x}(t) = 68,4, \quad (8)$$

with which, under the current initial conditions, we then "ran through" the PR forecast for the same cosmonauts in order to determine whether it could be used to predict the PR in future flights. The forecasting results were found to be satisfactory (see errors in Table 1) and for this reason equation (8) was also used to predict the PR of the two cosmonauts on Salyut-4. For the sake of comparison, we "ran through" the PR forecast for cosmonauts Nos 1, 2 and 3 by means of their individual models (7) under current initial conditions. All prognostic errors listed in Table 1 were calculated using the following formula:

$$\sigma^l(j) = \sqrt{\frac{\sum_{i=k}^N (x_{ji} - x_{ni})^2}{\sum_{i=k}^N x_{ji}^2}} \times 100\%, \quad (9)$$

where l is the index of model type (1, 2 or 3); j is the number of days for which the forecast was made; k is the number of flight days, starting at which the forecast was made; N is the number of days during which the forecast was made.

Table 1. Errors in forecasting cosmonauts' PR dynamics

$\sigma^l(j)$	Salyut-1			Salyut-4		Skylab-3		
	1	2	3	4	5	6	7	8
$\sigma^{1(1)}$	14,4	4,8	10,8	8,0	9,2	3,9	4,5	5,2
$\sigma^{1(2)}$				11,3	10,7	5,6	6,5	6,7
$\sigma^{1(3)}$				12,0	9,1	6,9	6,6	10,4
$\sigma^{2(1)}$	14,5	6,0	12,8					
$\sigma^{3(1)}$	12,8	5,8	12,4	11,4	13,0			
$\sigma^{3(2)}$				13,7	11,8			
$\sigma^{3(3)}$				9,5	14,2			
$\sigma_{m.e.}$	9,8	6,1	9,6					

Table 1 also indicates the prognostic errors made with regard to PR of cosmonauts Nos 1, 2 and 3 for 1 day, as predicted by a team of medical experts ($\delta_{m.e.}$).

The following conclusions can be derived from analysis of the errors:

- 1) Use of the method of extrapolation modeling in the class of differential equations is quite acceptable to solve tasks dealing with prediction of dynamics of physiological indices of cosmonauts in the course of prolonged flights, and the forecast error was close to the errors made by medical experts.
- 2) With increase in forecast time from 1 to 3 days, there is negligible change in error. This confirms the fact that the selected model, in the form of equation (3) describes rather well the dynamics of PR. For comparison purposes, along with model (3) we used algebraic polynomials to the power of 4÷7 to predict the PR of cosmonauts No 4÷8. In this instance, there was significant increase in errors with increase in number of days for which the forecast was made (5÷10% for 1 day, 10÷30% for 2 days and 30÷100% for 3 days).

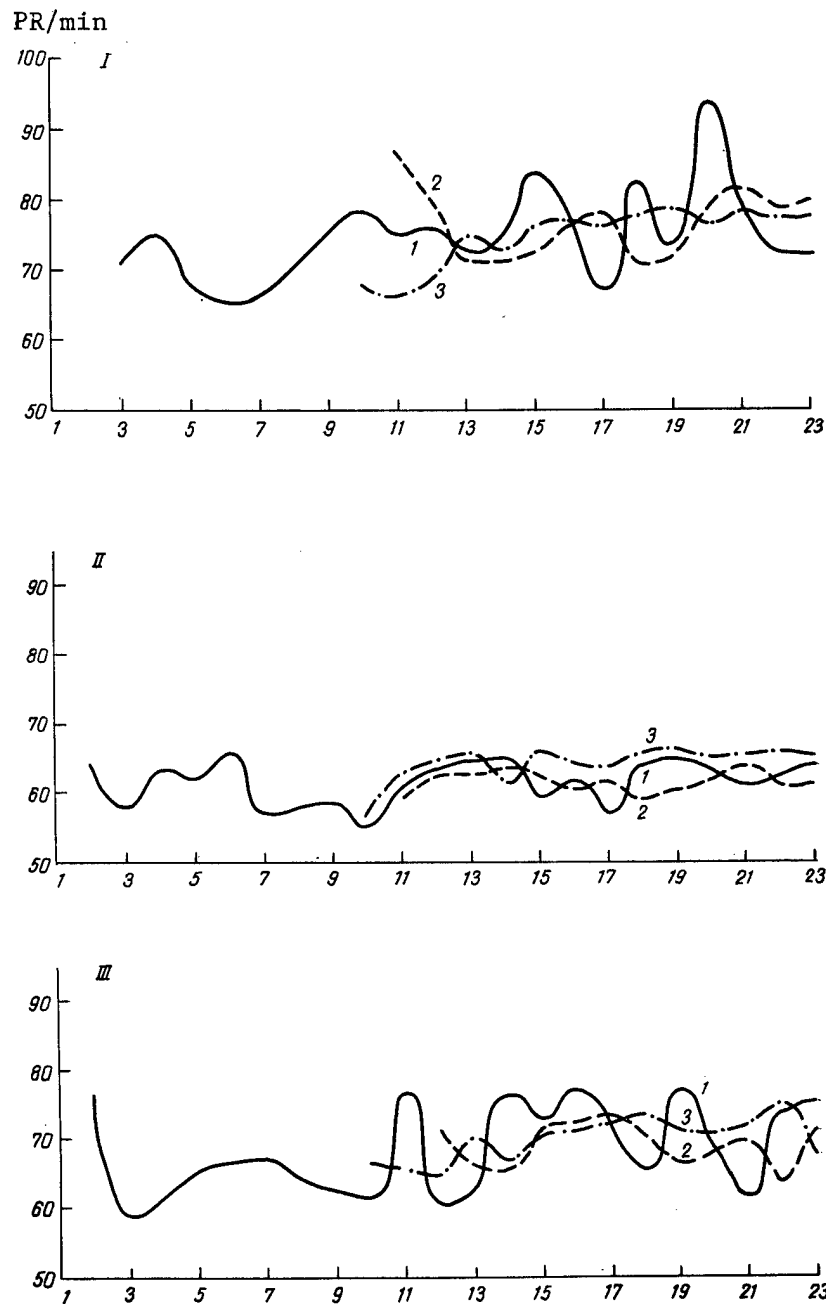


Figure 1. Prediction of PR 1 day ahead for crew of Salyut-1.
Top to bottom, cosmonauts Nos 1-3, respectively.

1) initial data 2) forecast with type 1 model 3) forecast of experts

3) The use of individual (type 2) and general (type 3) models to predict PR dynamics did not, on the average, yield an appreciable difference in number of errors, as compared to the use of current (type 1) models. The type 2 and

The figure consists of two vertically stacked line graphs, labeled I and II. Both graphs plot heart rate (PR/min) on the y-axis (ranging from 40 to 80) against time in minutes on the x-axis (ranging from 0 to 30). Three data series are shown in each graph: a solid line (1), a dashed line (2), and a dash-dot line (3).

Graph I: The solid line (1) starts at approximately 85 PR/min, decreases to about 65 PR/min by 10 minutes, and then fluctuates between 60 and 75 PR/min. The dashed line (2) starts at approximately 85 PR/min, decreases to about 65 PR/min by 10 minutes, and then fluctuates between 60 and 75 PR/min. The dash-dot line (3) starts at approximately 85 PR/min, decreases to about 65 PR/min by 10 minutes, and then fluctuates between 60 and 75 PR/min.

Graph II: The solid line (1) starts at approximately 70 PR/min, peaks at about 78 PR/min at 2 minutes, dips to about 60 PR/min at 4 minutes, and then fluctuates between 60 and 80 PR/min. The dashed line (2) starts at approximately 70 PR/min, peaks at about 78 PR/min at 2 minutes, dips to about 60 PR/min at 4 minutes, and then fluctuates between 60 and 80 PR/min. The dash-dot line (3) starts at approximately 70 PR/min, peaks at about 78 PR/min at 2 minutes, dips to about 60 PR/min at 4 minutes, and then fluctuates between 60 and 80 PR/min.

1) initial data 3) forecast using type 1 model
2) forecast using type 3 model

Parameters	Salyut-1			Salyut-2		Skylab-3		
	cosmonauts							
	1	2	3	4	5	6	7	8
T	2,22	1,68	1,48	1,0	1,08	4,09	1,41	2,23
ξ	0,46	0,70	0,60	0,56	0,19	0,25	0,22	0,13
t_p	14,7	7,0	7,3	5,0	17,0	25,0	10,0	26,0
Ω	15,6	14,8	11,6	7,5	6,9	25,8	8,8	13,5

60

in all cosmonauts during the flight: in cosmonauts No 5+8, there was marked fluctuation and the lower ξ ($\xi < 1$), the greater the fluctuation, while in the first 5, there was close to optimum fluctuation ($\xi_{opt} = 0.707$). Analogously, we were able to detect a difference in time of CVS adaptation to flight conditions. Of some interest are the data on damped fluctuations of PR, but the relatively short duration of the flights (23 and 28 days, if we disregard the American astronauts) and the small number of cosmonauts do not allow us to draw firm conclusions as yet concerning the existence of some typical biorhythms of the human heart due to space flight factors.

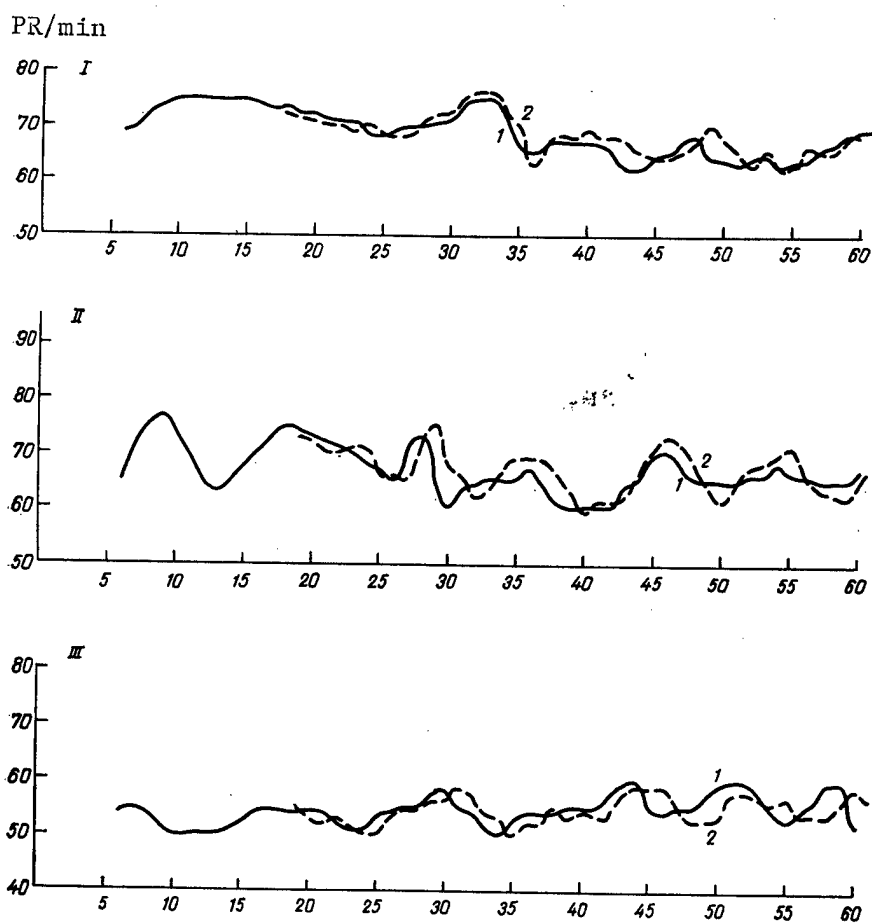


Figure 3. Forecast of PR for 1 day ahead on crew of Skylab-3; top to bottom, astronauts 6-8, respectively

1) initial data

2) forecast using type 1 model

In conclusion, we can state that the proposed mathematical system of analyzing the CVS of cosmonauts makes it possible to demonstrate important aspects of its function and to make a comparative analysis of efficiency of teams of cosmonauts involved in long flights.

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RESULTS OF METABOLIC STUDIES ON THE CREW OF THE SECOND EXPEDITION OF THE
SALYUT-4 ORBITAL STATION

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[Article by R. A. Tigranyan, I. A. Popova, M. I. Belyakova, N. F. Kalita,
Ye. G. Tuzova, L. B. Sochilina and N. A. Davydova, submitted 20 Feb 76]

[Text] The biochemical studies conducted according to the program of the second expedition of the Salyut-4 orbital station (OS) were directed toward extensive investigation of metabolism of the principal systems in the organism of a man who was exposed for a long time to the complex set of space flight factors, as well as changes observed at the early stages of readaptation to earth's gravity.

Methods

Venous blood (serum and plasma) and 24-hour urine specimens served as the material for biochemical studies. The preflight findings, obtained 87-89 days before the flight served as background data. Venous blood was tested once, while urine was collected for 2 days from P. I. Klimuk and 3 days from V. I. Sevast'yanov. In addition, 24-hour urine was collected on the launch pad, 1-6 days before the flight.

Venous blood was taken from the cosmonauts twice after the flight, on the 2d and 7th days. Urine was taken on the day the flight was completed and for the next 7 days.

The method of automatic analysis was used to assay the following indices: total protein, creatinine [9], urea [17], uric acid [19], glucose [16], chlorides [21], inorganic phosphorus [13], activity of the following enzymes: creatine phosphokinase--KF [Soviet pharmacopeia No] 2.7.3.2., alanine aminotransferase--KF 2.6.1.2., aspartate aminotransferase--KF 2.6.1.1. and alkaline phosphatase--KF 3.1.3.1 [18]. The fractional composition of proteins was determined by electrophoresis on acetate-cellulose; lactate concentration, using the reaction with paradiphenyloxide [7]; pyruvate, by the reaction with 2,4-dinitrophenylhydrazine [3]. Total lactate dehydrogenase (LDH) activity was determined by electrophoresis in polyacrylamide gel [5]. The concentration of epinephrine and norepinephrine in blood

[2] and 11-hydroxycorticosteroids (11-HCS) [4] was determined by the fluorometric method, and the radioimmune method was used to assay the concentration of insulin and thyroxine [14]. An assay was also made of excretion in urine of epinephrine, norepinephrine, dopa and dopamine [2], 17-ketosteroids [11], 11-HCS [33], 17-hydroxycorticosteroids (17-HCS) [22] and creatine [11].

Results and Discussion

As a result of the postflight examination, several changes were demonstrated, which were usually in the same direction and differed only in severity.

We found a significant change in concentration of blood urea and creatinine in cosmonauts who had completed a 63-day space flight (Figure 1). On the 2d postflight day, urea content (see Figure 1, top, unshaded columns) constituted 15 mg% in P. I. Klimuk and 19 mg% in V. I. Sevast'yanov, the background levels constituting 70 and 66 mg%, respectively, while blood creatinine (see horizontally striped columns in Figure 1, I) showed a 1.7-fold decline, as compared to background values (1.1 and 1.9 mg%) in P. I. Klimuk and 1.8-fold decline in V. I. Sevast'yanov (1.1 and 2.0 mg%). Concurrently, we observed decreased excretion of these substances in urine (with the exception of higher excretion of creatinine by P. I. Klimuk). The changes in other indices of protein and nitrogen metabolism were in the normal range. There was some increase in blood protein and uric acid, as well as decreased excretion of creatine in urine on the 2d postflight day and some increase in excretion thereof in V. I. Sevast'yanov. Special mention must be made of the fact that the cosmonauts presented a high level of uric acid excretion in urine in the preflight period, considerably higher than the conventional norm. This may serve as an indication of some activation of renal excretory function. The elevated excretion in urine of inorganic phosphorus and particularly chlorides, which were above the top of the normal range, indicated the validity of this assumption.

It had previously been shown in experiments on volunteer subjects [1] that prolonged hypokinesia leads to a change in processes of protein and nitrogen metabolism in the direction of a negative balance. These model experiments were confirmed by the results of previous space flights [13]. It was established that the lack of appreciable changes in rate of excretion in urine of the main products of nitrogen metabolism in the postflight test on the crew of the second expedition of the Salyut-4 OS warrants the belief that the level of catabolic processes in the cosmonauts' organism was normal immediately after completion of the space flight. In all probability, this is related to the system of physical conditioning and exercises that the cosmonauts followed throughout the flight.

It is known that the main sources of nitrogen-containing compounds (urea, creatinine, creatine) in urine are metabolic processes in muscle tissue. For this reason, the normal postflight level of these substances in urine may be interpreted as an indication of lack of significant changes in the muscular system. This assumption was confirmed by the results of testing the activity of several enzymes in the cosmonauts' blood. We refer, first of all, to creatine phosphokinase and the isozyme, LDH₅. Previously, it was

distinctly demonstrated [11, 18] that these enzyme systems are the most sensitive index of acute motor stress due to an increased muscle load. As we see in Figure 2, an insignificant increase, within the normal range, in creatine phosphokinase activity was observed only in V. I. Sevast'yanov, on the 2d postflight day; no changes in LDH₅ (fraction of muscle isozymes) activity was demonstrable in either P. I. Klimuk or V. I. Sevast'yanov.

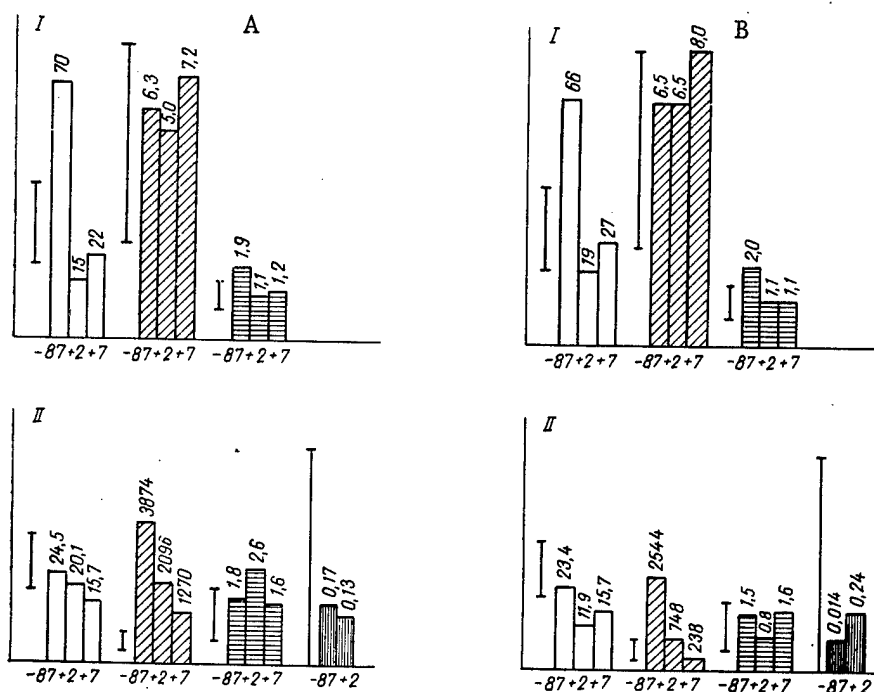


Figure 1. Comparative indices of protein and nitrogen metabolism of cosmonauts tested in the preflight (-87 days) and post-flight periods (2d and 7th days).

Unstriped columns: urea of blood (mg%, I) and urine (g/day, II)

Slanted stripes: uric acid of blood (mg%, I) and urine (mg/day)

Horizontal stripes: creatinine of blood (mg%, I) and urine (g/day, II)

Vertical stripes: creatine in urine (g/day)

Normal range is shown by the vertical lines to the left of each set of columns. In all of the figures, A refers to P. I. Klimuk and B, to V. I. Sevast'yanov.

The activity of other enzyme systems of human blood is tested extensively in clinical practice for the detection of a number of pathological changes referable to the myocardium, liver and kidneys. Figure 2 illustrates the results of analyzing activity of the following enzymes: alkaline phosphatase, creatine phosphokinase, alanine aminotransferase and aspartate aminotransferase. Among the most appreciable changes in enzyme activity after completing a space flight, we should mention the increase, in one crew member, in activity of both transaminases and alkaline phosphatase, which was marked, and in the case of the transaminases exceeded the physiological range. The

dynamics of changes in these enzymes in blood were, however, smooth in the crew commander. The data submitted warrant the assumption that, as a result of completing the 63-day flight, the flight engineer developed some functional tension referable to the hepatic system, as also indicated by the high level of pyruvic acid in blood, which was found in him on the same postflight days (Figure 3).

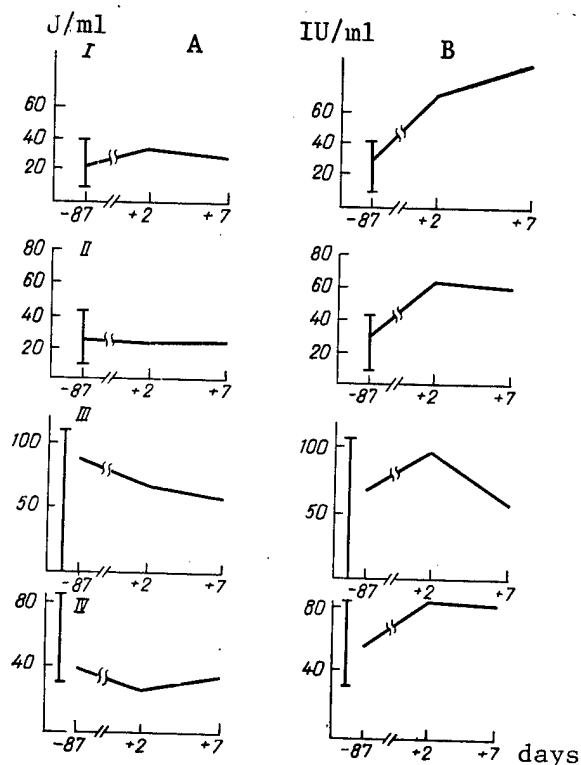


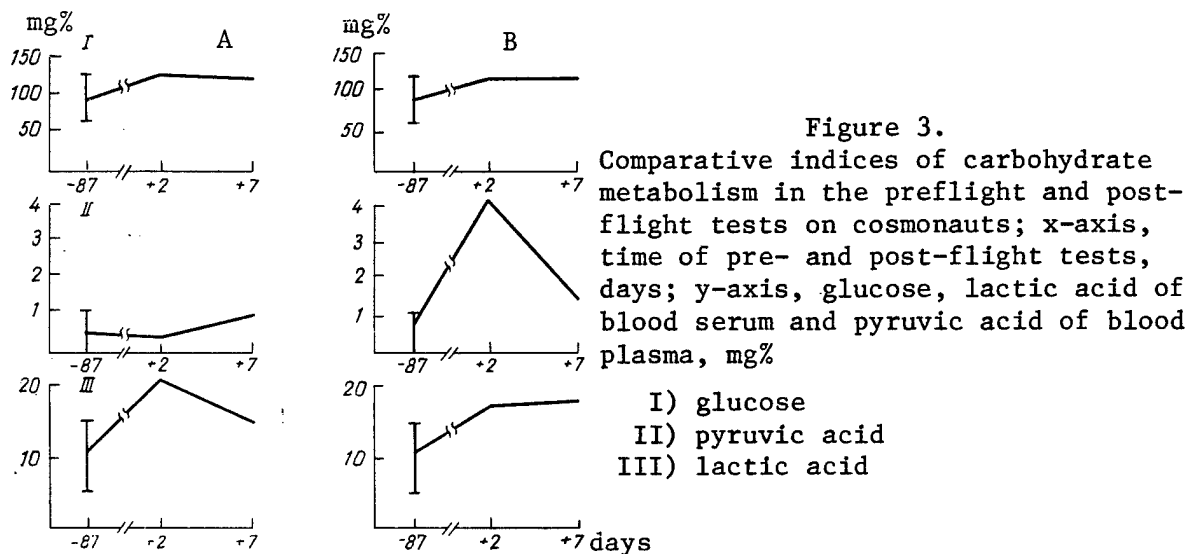
Figure 2.
Changes in blood serum enzyme activity in the pre- and post-flight periods; x-axis, time of pre- and post-flight tests, days; y-axis, enzyme activity, IU [international units]/ml

- I) alanine aminotransferase
- II) aspartate aminotransferase
- III) creatine phosphokinase
- IV) alkaline phosphatase

In previous experiments with hypokinesia [6], it was shown that blood and tissue lactic acid content increases already by the 15th-20th day of immobilization. The increase in lactate is the result of glycolytic breakdown of carbohydrates in the organism. As can be seen in Figure 3, a significant increase in concentration of lactic acid was found in both cosmonauts, in the postflight period.

Figure 4 illustrates the results of testing the sympathoadrenal system of crew members. Blood catecholamines did not exceed the physiological range in both cosmonauts, either before the flight or when tested in the post-flight period (with the exception of norepinephrine level on the 7th day in V. I. Sevast'yanov). Excretion in urine of norepinephrine, as well as dopa, was high both before and after the flight. There was a sharp increase in norepinephrine and dopa excretion in urine on the 4th postflight day and it remained high on the 7th day. This reaction of the sympathoadrenal system can be easily understood, if we consider that the activity of the medullary layer of the adrenals increases under the influence of diverse

physical and psychological stimuli. The moderate hyperglycemia, which we observed in the postflight period (see Figure 3) is probably the result of such activation.



Pre- and post-flight dynamics of hormone level changes in urine of cosmonauts

Index	Normal range	P. I. Klimuk									
		preflt. days		postflight days							
		88	87	0	1	2	3	4	5	6	7
11-HCS, $\mu\text{g}/24 \text{ h}$	30—96	69,6	65,5	43,6	47,7	38,4	61,6	46,5	68,0	104	170
17-HCS, total, $\mu\text{g}/24 \text{ h}$	4,67—7,02	4,66	6,01	6,34	10,14	8,04	18,87	12,6	9,11	8,98	7,60
17-HCS, bound with mineral acids, % of total	14—24	17	15	17	27	40	34	35	12	17	18

Index	Range	V. I. Sevast'yanov										
		preflight days			postflight days							
		89	88	87	0	1	2	3	4	5	6	7
11- HCS, $\mu\text{g}/24$	30—96	65,7	66,4	57,9	19,3	55,6	108	54,4	72,5	96,5	76,0	82,1
17- HCS, total $\mu\text{g}/24 \text{ h}$	4,67—7,02	5,48	5,75	6,0	2,52	14,45	9,92	26,6	12,84	7,44	6,73	6,1
17 HCS, bound with mineral acids, % of total	14—24	20	20	24	33	28	41	34	37	12	12	14

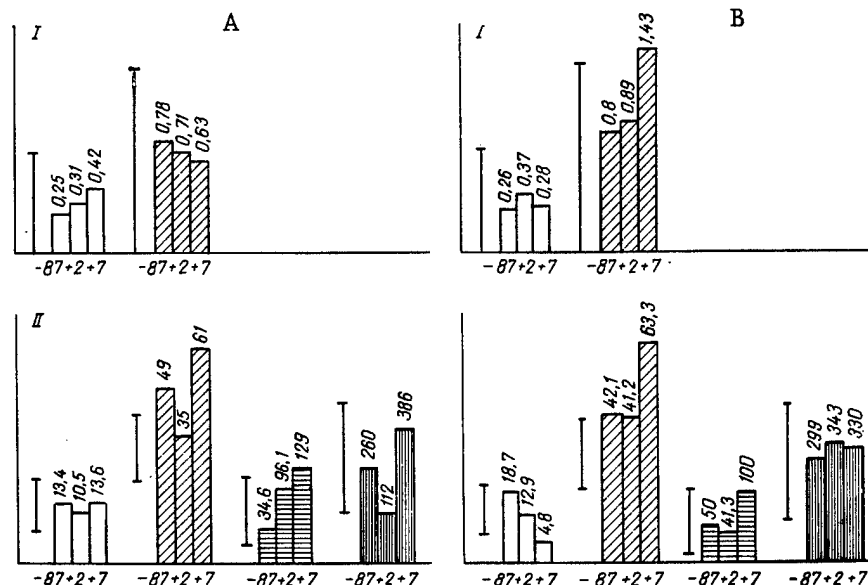


Figure 4. Levels of catecholamines and their precursors in blood and urine of cosmonauts in preflight (87 days before expedition) and postflight periods (+2 and +7 days after flight). Unstriped columns: epinephrine content in blood (μg%, I) and urine (μg/day, II) Slanted stripes: norepinephrine of blood (μg%, I) and urine (μg/day), II) Horizontal stripes: dopa content of urine (μg/day) Vertical stripes: dopamine content of urine (μg/day)

Along with the change in function of the adrenal medullary layer, some changes were also noted in the crew of the second expedition of Salyut-4 OS with reference to indices characterizing the function of the adrenal cortex. The most significant changes in levels of these hormones in urine are listed in the Table. American researchers had reported, even earlier, that there was a significant increase in excretion of 17-HCS in urine in cosmonauts that had participated in long space flights. An appreciable increase in total 17-HCS content of urine was demonstrated in both cosmonauts in all postflight tests (with the exception of a low level of 17-HCS in urine of V. I. Sevast'yanov on the day he landed). A study of fraction composition of 17-HCS revealed that the observed increase in total corticosteroids in urine was probably due to a significant increase in mineral-acid-bound fraction of 17-HCS (from 14-24%, which is normal, to 40-41% on the 3d post-flight day in both cosmonauts). The increase in level of this 17-HCS fraction is probably due to activation of enzyme systems of the liver, which implement conjugation of corticosteroids with mineral acids.

The dynamics were somewhat different, with respect to changes in excretion of 11-HCS in urine: after some decrease in excretion of these hormones in urine, on the day both cosmonauts landed and for the next 2-3 days there was an appreciable increase in excretion of 11-HCS. In P. I. Klimuk, levels

thereof exceed the physiological range on the 6th and 7th postflight days. The changes in 17-ketosteroid content of urine, as well as insulin and thyroxine of blood were negligible at all tested postflight times (with the exception of some elevation of blood thyroxine in P. I. Klimuk on the 2d day after the flight). Consequently, on the basis of the data obtained, we can merely refer to some activation of glucocorticoid function of the cosmonauts' adrenal cortex.

Thus, as a result of this study, it was clearly demonstrated that the 63-day space flight had no appreciable effect on metabolism, according to the indices tested on the crew of the second expedition of Salyut-4 OS.

In this study, we failed to demonstrate any adverse biochemical changes that would preclude longer manned space flights. However, identification of mechanisms responsible for many of the observed changes requires further investigations.

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EFFECTS OF 22-DAY SPACE FLIGHT ON LYMPHATIC ORGANS OF RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 53-57

[Article by G. N. Durnova, A. S. Kaplanskiy and V. V. Portugalov, submitted
11 Apr 75]

[Text] The objective of this work was to investigate the effects of space factors, and first of all of weightlessness, on the system of lymphatic organs with hemopoietic and immunocompetent functions. It was necessary to conduct such a study because, until recently, all information concerning the influence of space flights on mammalian lymphatics was limited to post-flight findings on mice after a 24-hour flight around the earth in Sputnik No 2 [1, 3].

Methods

The material we studied consisted of the spleen, thymus and inguinal lymph nodes of 14 rats that had spent 22 days onboard the artificial earth satellite, Kosmos-605 and were sacrificed 2 and 27 days after this flight, and 12 rats from a ground-based model experiment, in which all of the space flight conditions, with the exception of weightlessness, were simulated, also sacrificed at the same times. The lymphatic organs of 28 rats kept in a vivarium for the duration of the experiment served as a control.

The organs of experimental and control animals were weighed, fixed in Carnoy fluid or 10% neutral formalin, and imbedded in paraffin. Sections of these organs were stained with hematoxylin and eosin, methyl green, pyronine and picrofuchsin; the Perls method was used to demonstrate iron in the spleen sections.

Smears were prepared of spleen cells, they were fixed in absolute ethanol and stained by the Peppenheim method to analyze the splenograms. We counted 400 cells in each smear.

In order to determine the proportion of white and red pulp in the spleen, sections of the latter, made perpendicular to the organ's long axis, were photographed and determination was made of the area of the cross section of

the spleen and area of white pulp on enlarged negative projections, using a planimeter. The area occupied by red pulp was estimated by subtracting the area of white pulp from the area of the spleen's cross section.

All of the digital data obtained were submitted to statistical processing. Differences in results obtained were considered reliable with $P < 0.05$.

Results and Discussion

According to the data given in the Figure, there was significant decrease in weight of the spleen and thymus of rats sacrificed 2 days after the space flight, while the decrease in weight of inguinal lymph nodes was statistically unreliable. The weight of the spleen and thymus of experimental animals was restored on the 27th postflight day, and did not differ from the data for the control group of rats.

Unlike the animals in the flight group, rats sacrificed 2 days after the ground-based experiment presented only a decrease in weight of the spleen. The weight of the thymus and inguinal lymph nodes did not change. The weight of all lymphatic organs, including the spleen, did not differ from the control 27 days after completion of the ground-based experiment.

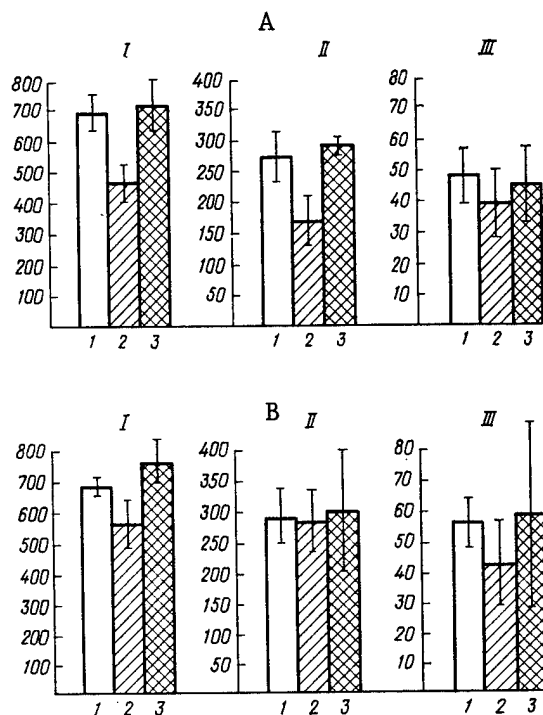
As shown by morphometric studies, the decrease in spleen weight of rats sacrificed on the 2d postflight day was due to hypoplasia of red and white pulp of the spleen, and the area of white pulp showed a 21% decrease, that of red pulp, a 19% decrease, as compared to the control. Restoration of spleen weight in rats of the flight group 27 days after returning to earth occurred primarily due to hyperplasia of red pulp, while hypoplasia of white pulp still persisted.

The changes in the spleen of rats in the ground-based experiment were analogous to those in the flight group, but less marked quantitatively.

Histologically, the spleen of the rats in the flight group, sacrificed 2 days after landing, showed a decreased number of cellular elements in red and white pulp. Foci of erythroid hemopoiesis disappeared and there was a decrease in number of blast forms and lymphocytes in the red pulp; in the white pulp, there was a decrease in number of small lymphocytes, which constitute the bulk of lymphoid follicles, and decrease in number of blast and dividing forms in the clear centers of lymphoid follicles. In addition to hypoplasia of red and white pulp, intensive accumulation of hemosiderin in the spleen was a typical histological finding.

In the flight group of animals sacrificed 27 days after returning to earth, we found activation of proliferative processes in red and white pulp, with intensification of erythroid hemopoiesis in red pulp and increase in number and size of clear centers of lymphoid follicles in white pulp; in these follicles there was appearance of many blast and dividing cells. In spite of activation of proliferative processes in the clear centers of lymphoid follicles, their mantle region, consisting of small lymphocytes, remained

narrower than in control animals. As compared to animals sacrificed on the 2d postflight day, the amount of hemosiderin in red pulp of the spleen diminished considerably more and was only slightly above the level in control animals.



Changes in weight of lymphatic organs of rats after the 22-day space flight (A) and ground-based experiment (B). Data were submitted to statistical processing by the method of confidence intervals with $P = 0.05$.

- I) spleen
- II) thymus
- III) lymph nodes
- 1) vivarium control
- 2) 2 days after end of experiment
- 3) 27 days after end of experiment

Qualitatively, the histological changes in the spleen of rats sacrificed 2 and 27 days after the ground-based experiment were identical to those in the flight group, but quantitatively they were considerably less marked.

The results of cytological examination of the spleen revealed that there was a statistically reliable decrease in number of immature elements of the lymphocyte (by 37%), plasmocyte (by 59%) and erythroid (by 94.2%) classes and increase in segmented neutrophils (by 150%) 2 days after completing the flight. After 27 days, the number of immature lymphocytic and plasmocytic elements reverted to normal, while the number of mature plasmocytes was even somewhat above normal (by 42%). There was a particularly sharp increase in number of erythroid cells in the spleen (5 times more than in the control).

Unlike the flight group of animals, the splenogram of rats sacrificed on the 2d day after the ground-based experiment did not differ appreciably from that of control animals, while in rats sacrificed on the 27th day, we were only able to detect an increase in number of plasmocytes and a tendency toward increase in number of normoblasts.

Histological examination of the thymus and inguinal lymph nodes of rats sacrificed on the 2d day after landing revealed that a 22-day stay in the spacecraft led to hypoplasia of these organs, due to decrease in number of

lymphocytes in the cortex of the thymus and lymph nodes. In addition to the decrease in lymphocytes in the cortical substance of the thymus and clear centers of lymph nodes, immature cell forms with pyroninophilic cytoplasm, as well as dividing cells, were encountered considerably less often than is normal. The structure of the thymus and inguinal lymph nodes reverted to normal 27 days after the space flight, while activity of proliferative processes in the clear centers of the lymph nodes was even somewhat above normal.

No morphological changes were demonstrated in the thymus of rats sacrificed 2 and 27 days after the ground-based experiment, as compared to the control group. There was some decrease in number and size of clear centers in the inguinal nodes of rats sacrificed on the 2d day after the ground experiment, but there was complete recovery after 27 days.

Analysis of the submitted data warrants the belief that a prolonged space flight leads to hypoplasia of lymphatic organs, with greater decrease in weight of the spleen and thymus and considerably less decrease in weight of inguinal lymph nodes. The reduction of lymphoid tissue is apparently related to development of a stress reaction, since it is known that space flight factors, such as accelerations, restricted motor activity and hyperoxia, may elicit development in animals of the systemic adaptation syndrome with its inherent hyperfunction of the adrenals and hypoplasia of lymphoid tissue [2, 4-6]. Since we failed to demonstrate a decrease in weight of the thymus (as we know, its cells are the most sensitive to increased levels of corticosteroids, and weight decreases primarily with development of "stress") in the ground-based experiment, which simulated space flight conditions, with the exception of weightlessness, it can apparently be assumed that expressly weightlessness is the chief etiological factor in development of "stress."

The hypoplasia of lymphatic organs and reduction in number of mature lymphocytes in lymphoid organs, which we demonstrated, is quite consistent with the findings of postflight examinations of cosmonauts, which revealed that lymphopenia was present in blood, under the influence of space flight factors.

As we have already mentioned, along with decrease in number of lymphocytes in the spleen of rats in the flight group, we observed inhibition of erythroid hemopoiesis and intensification of erythrocyte breakdown. This phenomenon may be based on several causes, the most probable being the high oxygen content in the atmosphere of the Kosmos-605 and restricted motor activity of the animals, or, as shown by ground-based experiments [4, 5], these factors elicit depression of erythropoiesis and accumulation of hemosiderin in the spleen. At the same time, we cannot rule out the possibility that weightlessness could also depress erythropoiesis in the spleen, since this was considerably more marked in rats on Kosmos-605 than in animals in the ground-based experiment. In the light of the obtained data, it is understandable why a decrease in erythrocyte mass was found in American astronauts following long space flights [7, 8]. This decrease is apparently related to both depression of erythroid hemopoiesis and intensification of erythrocyte breakdown, due to the combined effect of hyperoxia, weightlessness and restricted motor activity.

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INTESTINAL AUTOFLORA OF TEST SUBJECTS IN THE COURSE OF A 6-MONTH BIOENGINEERING EXPERIMENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 57-59

[Article by M. S. Rerberg, N. S. Manukovskiy and L. A. Somova, submitted
11 Jun 74]

[Text] In recent years, as a result of experiments with self-contained life-support systems, a significant amount of data has been obtained on the effect of isolation on human intestinal flora. It has been established that the species composition of the flora becomes simpler [6, 13] and its pathogenic properties increase [4] when people are kept in a closed space for long periods of time. It was shown that emergency situations affect the number of different groups of intestinal bacteria [7].

In this work, we studied the intestinal microflora of four subjects [investigators] who stayed in a BIOS-3 closed system of life support for a long time. Our objective was to determine the effects of conditions in the BIOS-3 system on the intestinal microflora of man. I. A. Terskov et al. have given a brief description of BIOS-3 [5].

Method

The studies were continued for 6 months (180 days). Subject T. remained in the BIOS-3 system for the entire 6 months, P., for the first 3 months, B. for the last 4 months, and Sh. for the first 2 and last 2 months. They were all on a mixed diet. Part of the food was delivered from the outside in lyophilized form, and the rest (bread, vegetables) was provided as a result of recycling [cycle] of matter in the system.

We studied the intestinal microflora in specimens of feces that were collected for 3 successive days each month. Cultures were made within 15-30 min after defecation.

All of the subjects presented normal microflora before the experiment.

We used the "hourglass" method of Haenel [9] to isolate asporulated anaerobic bacteria. Blood agar was used for overall counting of anaerobes. Bacterioids were estimated on Haenel medium No 4 with neomycin, bifidobacteria on Haenel medium No 5 with lactose, and sporulated anaerobic *Clostridium perfringens*, on Wilson-Blair medium. We used the droplet method of Haenel, Muller-Beuthow [10], as modified by Heyde [11] to count aerobic bacteria. *Colibacilli* were counted on Endo medium, enterococcus on Kalina medium, staphylococcus on Chistovich's yolk and salt agar, proteus on a medium with urea, according to Haenel, Muller-Beuthow [10], and lactobacillus on MRS-4 medium with 0.04% sorbic acid by the method of A. A. Lentsner [3].

We counted the amount of microorganisms per gram wet feces weight and reported in logarithms of absolute numbers.

Results and Discussion

Bacterioids were notable for large and most stable number in the course of the experiment. There were also minor changes in total number of microorganisms per gram feces ($\log x \pm I_{95}$)*: 9.1 to 10.2, 9.6 to 10.4, 9.2 to 10.4 and 9.4 to 10.4 in subjects T., P., B. and Sh., respectively. This confirms the existing view that the intestinal autoflora is stable in size [2, 14].

Statistically reliable fluctuations in size of different groups of microorganisms appeared more or less simultaneously in different subjects, starting in the 3d month of the experiment. Thus, in subject T., both the lowest (4.2 log/g, 3d month) and highest (6.8 log/g) number of microorganisms were demonstrated at this time in the proteus group. There were significantly more sporulated anaerobes than in the background: 6.4 log/g (4th month), versus 3.55 log/g in the background. Virtually analogous changes in putrefactive microflora were observed in subjects P. and B. There were individual elements in the nature of fluctuation of enterococci; however, they were present in largest number midway through the experiment. In all subjects, the increase in number of representatives of putrefactive flora occurred against the background of lower frequency of defecation and development of certain other static signs in the intestine. Addition to the diet of inert matter, mainly cellulose, in the 5th and 6th months normalized the function of the intestinal tract and lowered the number of putrefactive organisms in the specimens.

The number of so-called transient staphylococcal microflora and yeast in the specimens examined fluctuated over a wide range, from 0 to 10^4 cells/g with no particular pattern. Such fluctuations of "transient microflora" may also be demonstrated in healthy people under ordinary circumstances. In all of the subjects, there was a decrease in number of bifidobacteria and lactobacilli. This inevitable consequence of isolation, which had been previously detected by V. M. Shilov et al. [6] in a year-long medicoengineering

* I_{95} is the confidence interval of the logarithm of geometric mean for 95% probability.

experiment, is particularly dangerous, since it results in impairment of normal, eubioengineering proportions of intestinal microflora, which could be the cause of avitaminosis and endogenous infections [12]. The instability of microflora during the experiment is indicative of inadequate conditions of the experiment to man. Since we were unable to relate this inadequacy to the effect of any single factor, it was apparently due to both causes inherent in closed systems (restricted mobility, very marked decrease in influx of exogenous microflora, psychological effect of prolonged isolation) and those inherent only in this experiment: uniqueness of ambient microorganisms, gas composition of air inhaled by the people. In particular, in the 3d-4th and beginning of the 5th month, we observed accumulation of CO and CO₂ in the atmosphere of the system. Prolonged exposure to the latter, in concentrations of 1-1.5 to 2.3%, could elicit significant strain on defense and adaptation functions of the human body, as was shown by Schaefer [15], against the background of a satisfactory condition and in the absence of perceptible deviations with reference to behavioral reactions. Furthermore, there are data indicative of the more toxic effect of CO, the concentration of which for some short periods reached 0.04 mg/liter, in the combined effect of CO and CO₂ [1].

In this experiment, none of the indices tested, with the exception of minute volume [of respiration], presented reliable changes that could be indicative of deviations of the individuals' physiological status from normal. For this reason, the dynamics of intestinal microflora demonstrated during the above-mentioned adverse period are indicative of high sensitivity thereof to change in equilibrium between the human body and the environment. Analysis of dynamics of *Clostridium perfringens* is indicative of a link between this microorganism and lipid metabolism, as was previously noted by Graber et al. [8], in experiments on animals. This link is particularly well demonstrable between the increase in total lipids, decrease in blood lipase activity and increase in number of *Clostridium perfringens* cells in the feces of subject T.

Thus, the dynamics of size of different groups of intestinal microorganisms demonstrated in the course of our experiment are indicative of the fact that the environment formed by the BIOS-3 closed system of life support is not absolutely adequate for man. Since the environmental inadequacy was demonstrated chiefly with reference to intestinal microflora, the latter can be considered a rather sensitive indicator of the state of equilibrium between the human body and the environment.

In spite of the instability of intestinal microflora at different periods and the tendency toward simplification thereof, the overall number of microorganisms per gram specimen was relatively stable in all subjects. The bacterioid group was the most stable and present in largest number; staphylococcus and yeast were the least stable and fewest in number.

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RHEOGRAPHIC STUDY OF THE HUMAN CARDIOVASCULAR SYSTEM WITH EXPOSURE TO
HIGH PRESSURE FOR MANY DAYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by L. I. Ardashnikova and L. A. Chudnovskaya, submitted 30 Sep 74]

[Text] Studies of the cardiovascular system with exposure to hyperbaric conditions were conducted primarily with elevated PO_2 . Some authors reported that, at rest, with brief exposure to elevated PO_2 (up to 2 atm), the pulse rate diminishes [3, 5, 6, 10, 13, 17, 20, 25]. However, some researchers observed a faster heart rate (HR) [24]. When working under elevated PO_2 , a slower pulse rate is observed, as compared to working under the usual pressure [21, 25, 26].

It has been reported that oxygen has a vasoconstrictive effect, at rest, on cerebral and peripheral vessels. This is associated with some elevation of arterial pressure, particularly diastolic [3, 14, 18, 19].

The present study was undertaken on the premise that, in the presence of elevated pressure and respiration of compressed air or nitrogen and oxygen mixtures, changes occur in various vascular regions and, first of all, in the pulmonary circulatory system due to the higher density of the gas environment.

It is difficult to study human circulation under such conditions, because it is impossible to use a number of the methods ordinarily used in clinical practice. Rheography, which permits examination of regional circulation and cyclic changes in blood-filling of the organ under study during cardiac contractions, is one of the most suitable methods under these conditions.

Methods

This investigation was pursued on 6 essentially healthy males ranging in age from 28 to 35 years, who had undergone a special medical examination. Two men worked on a bicycle ergometer with a force of 900 kg-m/min for 10-12 min, until HR rose to 180-190/min; 4 men pedaled with increase in load in steps (300, 450, 600, 750 and 900 kg-m/min, each step lasting 5 min, with 3-min intervals). In addition, 2 men worked on the ergometer,

increasing force of pedaling at will, to the level of maximum oxygen consumption (MOC) in the last, 5th, min of exercise, and 2 others pedaled at the rate of 900 kg-m/min for 12-15 min.

We recorded the following: rheoencephalogram in the bifrontal lead, longitudinal rheogram of the leg (lead electrodes applied over the lower and upper third of the leg) and rheogram of the lung (1.5×1.5 cm electrodes applied according to Pushkar': anteriorly to the midclavicular line in the second intercostal space and on the back, a 6×8 cm electrode was placed along the scapular line). Rheograms and one EKG lead according to (Nebu) were recorded at rest and after pedaling on the ergometer for 20-30 s, then for 15-20 min of the recovery period.

The artificial gas environment in which the subjects remained for 7 days, had the following parameters: 5 atm(abs) total barometric pressure; 3398-3427 PN₂; 350-380 mm Hg PO₂; 6-8 mm Hg PCO₂; 24-26° temperature of gas environment.

Thus, the subjects were exposed concurrently to high pressure, moderate hyperoxia and high PN .

Results and Discussion

The main index of pulsed fluctuations in filling of the region under study is the rheographic index (RI), i.e., the ratio of amplitude of the rheographic wave to the calibration signal, did not undergo consistent changes, as compared to an environment of 1 atm(abs), in all of the tested regions at rest, under high pressure. The magnitude of the index of pulsed delivery of blood (PDB) and product of RI multiplied by HR, for the brain and lung under pressure of 5 atm(abs) at rest, did not differ from the indices at 1 atm(abs) (the differences are unreliable, $P > 0.1$).

After pedaling at 1 atm(abs), the RI of the leg rose, which is consistent with previously published findings [9], and apparently it is related to an increase in systolic volume, as well as decreased tonus of resistive vessels of the leg. The PDB increased even more after exercise. However, at 5 atm(abs) this increase was somewhat less marked. In view of the fact that, according to several indirect signs, cardiac output while performing vigorous work under pressure is not lower, but probably even higher, than at 1 atm(abs), we cannot rule out the possibility that the minor decline of the PDB index is related to an increase in continuous flow of blood in the peripheral vessels. However, there is more plausibility to the hypothesis that, in spite of the increase in cardiac output, the RI of the leg increased when pedaling at 5 atm(abs) to a lesser extent than at 1 atm(abs), due to the fact that there is less decrease in vascular tonus when exercising at 5 atm(abs) than 1 atm(abs). This could lead to more marked humoral changes, in particular, acidosis in the working muscles. This interpretation of the data obtained is confirmed by the fact that, in several subjects, the dicrotic notch on the rheovasogram of the leg, under hyperbaric conditions, shifted toward the periphery of the dicrotic region and isoline 2-3 min after stopping work, which is indicative of a significant lag in lowering of vascular tonus in the working limb.

This study revealed that the RI and index of blood delivery to the brain, as well as to the leg, differ little at rest under 5 atm(abs) pressure. However, there were rather significant fluctuations of the index on different days. After exercise, the increase in RI and PDB to the brain was more marked under hyperbaric conditions in four out of the six subjects (see Table).

Index of blood delivery to the brain 30 s after exercising

<u>Subject</u>	<u>1 atm(abs)</u>	<u>5 atm(abs) on different days</u>
B.	103	112, 193, 161
S.	146	268, 224, 282, 151
M.	154	198, 230, 271
R.	210	138, 270
K.	360	532, 245
Ya.	136	216, 468

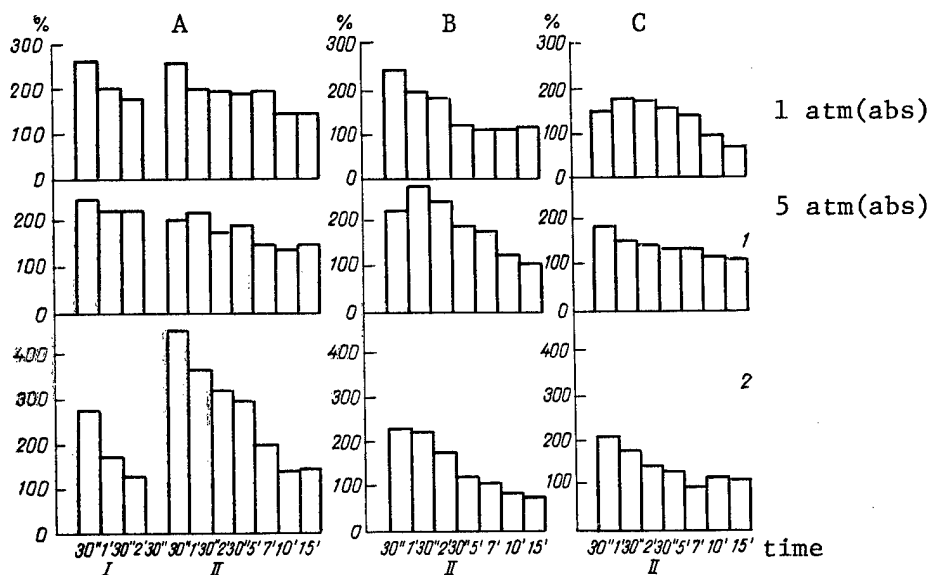
We detected significant individual fluctuations. Thus, in subject B., there was greater increase in PDB to the brain after exercising in steps at 5 atm(abs) than 1 atm(abs). However, on the 2d day of exposure to 5 atm(abs), it was less marked than on subsequent days under the same pressure, particularly after exercising on the highest level, 900 kg-m/min. In subject S., there was a greater increase of PDB on the 2d day of exposure to 5 atm(abs) after work constituting 750 and 900 kg-m/min than at 1 atm(abs), with subsequent decrease by the 7th day of exposure to 5 atm(abs). After exercising to the MOC level, we observed some individual distinctions to the PDB changes: in subject K., a greater elevation of the PDB index with reference to the brain was observed on the 2d day of exposure to 5 atm(abs); in subject Ya., at 5 atm(abs) it was essentially the same as at 1 atm(abs).

We should call attention to the difficulties involved in analyzing the above data, due to the inevitable instability of rheographic indices on different days. Still, we can conclude that PDB to the brain is not usually decreased and in most cases even increased under the influence of high pressure after various levels of physical loads, as compared to exercise at 1 atm(abs).

In view of the well-known increase in cerebral circulation under the influence of CO₂, one would think that the increase in ambient CO₂, which occurred in the first 2 groups of subjects, did not elicit an increase in rheographic indices at rest, since there was no significant arterial hypercapnia in these experiments. By contrast, during an exercise load under 5 atm(abs), hypercapnia was more marked and the changes in the rheoencephalogram were indicative of greater increase in PDB to the brain than at 1 atm(abs). As shown by the results of other investigations [7, 15], in this experiment, oxygen consumption, CO₂ discharge and acidoses were higher at 5 atm(abs) than with the same load at 1 atm(abs).

The rheogram of the lung, which reflects PDB to the pulmonary artery and its branches [2, 4, 11], failed to present appreciable changes at rest with exposure to hyperbaric pressure for many days.

After exercise, the lung RI and PDB changed at 5 atm(abs). As can be seen in the Figure, in subject Ya., after exercising to maximum oxygen consumption, the increase in PDB was more marked at 5 atm(abs) than 1 atm(abs), and it increased with increase in exposure to hyperbaric pressure, being higher on the 5th day than on the 2d. However, in some subjects, the higher PDB values of the first few days decreased toward the end of exposure to high pressure (subject M.) or did not change (subject B.).



Index of pulsating delivery of blood to the lung
X-axis, time after exercise; y-axis, magnitude of PDB, % of initial level at rest, before exercise

A) subject Ya.

B and C) subjects M. and B., 900 kg-m/min exercise

I) warmup

II) work to MOC

1) 3d day

2) 6th day

It may be assumed that the relative decrease of PDB in some subjects after exercising, toward the end of the period of exposure to hyperbaric pressure, is indicative of increased resistance of pulmonary vessels. This is also indicated by estimates of changes in the so-called slow component of the anacrotic wave on the lung rheogram. This index, i.e., time between maximum of first anacrotic derivative to peak of anacrotic wave, yields early information about the initial stages of increased resistance in the pulmonary circulation [12]. The slow component of the anacrotic wave was longer in some of the subjects. This could be related to the adverse effect of respiratory fluctuations of thoracic pressure on pulmonary circulation, which were increased due to the higher density of the environment. This assumption is quite consistent with the EKG signs of pulmonary hypertension: increase in amplitude of P wave on the EKG [1] and some typical changes in the anacrotic wave on the lung rheogram, which appeared in 4 subjects when exercising at 5 atm(abs).

In addition, we performed the so-called postural test, which is used in clinical practice with reference to vascular pathology [8]. The test consists of the following: a rheogram of the leg was taken with the subject in horizontal position, supine, after which the legs are passively elevated to a 45° angle and another rheogram is taken. In healthy individuals, when the leg is elevated under normal conditions, there is an increase in amplitude of the anacrotic wave on the rheogram. In 3 out of 4 subjects, in whom this test was normal at 1 atm(abs), there were significant changes at 5 atm(abs): instead of an increase in rheogram amplitude after elevating the leg there was a decrease in 3 subjects, and in 1 subject it did not change.

At the present time, it is difficult to determine the exact cause of such significant changes in the postural test at 5 atm(abs), but, at any rate, such a distortion of the reaction is indicative of diminished capacity to lower vascular tonus at 5 atm(abs), and it is probably indicative of a change in regulation of vascular tonus in the limb. It should be stressed, that during decompression the response to elevation reverted to normal. Consequently, the observed distortion is unrelated to the prolonged stay in a relatively small closed area, but that it is the result of conditions that develop in the course of prolonged exposure to hyperbaric pressure and an N₂-O₂ mixture.

Thus, on the basis of these investigations, it can be concluded that the rheographic changes at rest are minor with exposure to high pressure. Under such conditions, after exercise, they are significant and indicative of a greater strain on the cardiovascular system than the same exercise at 1 atm(abs). Evidently, a significant increase of P_O₂ in the environment does not relieve the load on the cardiovascular system while exercising at 5 atm(abs) and it was overlapped by the effects of other factors: higher density of gas environment, related increase in respiratory function, etc. We can also mention the manifestations of impaired regulation of vascular tonus, with a tendency toward increase thereof, in both the pulmonary and systemic circulation.

It must be stressed that we obtained our data under conditions involving exposure for many days to a pressure of 5 atm(abs) in an N₂-O₂ environment. Here, the air P_O₂ did not exceed 350-380 mm Hg, and p_O₂ of arterial blood was of the order of 110 mm Hg [15]. Of course, in the case of greater physical loads, a minor elevation of arterial p_O₂ would not necessarily reduce the strain on the cardiovascular system during exercise, which is usually observed when breathing pure oxygen at 1 atm(abs). At the same time, the factor that made exercising more difficult, namely, the higher density of the gas environment, was more significant than at lower pressure. Thus, our findings are important primarily for evaluation of the status of the cardiovascular system when working in a high-density environment and in the presence of relatively minor elevation of p_O₂ of arterial blood.

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EVALUATION OF EFFECTIVENESS OF MUSCULAR ELECTROSTIMULATION FOR THE PREVENTION
OF DISORDERS RELATED TO PROLONGED RESTRICTION OF MOTOR ACTIVITY IN MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 64-68

[Article by M. A. Cherepakhin, L. I. Kakurin, Ye. I. Il'ina-Kakuyeva and
G. T. Fedorenko, submitted 24 Feb 75]

[Text] Bed rest was the model of weightlessness. The Tonus-2 apparatus
was used for electrostimulation. Two series of studies were pursued, each
lasting 7 weeks. The subjects were healthy males who stayed in bed in an
antiorthostatic position (the head was 4-6° lower than the feet).

In the first series, 12 subjects were divided into 3 groups of 4 men each,
the first was a control, and the other two were stimulated with 20 (ES-20)
and 12 (ES-12) electrodes.

The reason for the different number of electrodes is that two versions of
application thereof were tested.

The muscles of the legs, thighs, abdomen and back were stimulated. Stimula-
tion lasted 25-30 min. In the first experiment, it was delivered in the
morning and evening, and in the second, once a day.

In the second series of studies, we evaluated the efficacy of electrostimula-
tion of muscles combined with physical exercise. There were nine subjects
in this series. As in the first series. they were divided into three
groups, with three people in each: a control (1st) and groups stimulated
before (2d) and after (3d) physical exercise.

The exercise consisted of pedaling on a bicycle ergometer with the subjects
in antiorthostatic position (the head 6° lower than the feet).

They exercised twice a day, in the morning and afternoon. In the morning
they pedaled uniformly with a load of 600 kg-m/min for 20 min. For the
1st 2 weeks, the afternoon exercises were performed with a load of 600-
700 kg-m/min for 60 min, then, starting with the 3d week, they exercised
intermittently: 3-min periods of pedaling, with a pulse rate of 140-170/min,
alternated with a rest period until the pulse rate dropped to 120/min. As

the intensity of exercise increased, its duration decreased. In the 7th week, the subjects exercised for 30 min and their pulse rate reached 170/min. At all stages of exercise, the energy expended on it was constant, constituting 500 kcal.

Before the start of the tests, biopsies were taken from the right soleus of muscle tissue for histochemical analysis. On the 30th day of the first series of studies and after the second, samples of muscle tissue from the same muscle of the left foot were taken from all subjects.

The physical fitness of the subjects was tested by means of functional tests before and after the studies. We used pedaling on a bicycle ergometer as the load. After recording initial indices, the subject would pedal for 5 min with a load of 600 kg-m/min in "sitting" position, then, starting in the 6th min, the load was increased by 100 kg-m each min until the subject was totally fatigued.

We recorded the time during which the subjects were capable of performing increasingly strenuous pedaling, as well as the heart rate according to the EKG. In the second investigation, using an automatic gas analyzer, we determined maximum oxygen consumption and consumption per unit body weight. We also determined static endurance of muscles according to time of retaining specified positions.

Results and Discussion

First series of studies: Histochemical tests revealed that there was a statistically reliable increase in size of red and white muscle fibers in the soleus of all four subjects in the control group.

In the 2d group of subjects, the muscle fiber size either remained unchanged or increased (with individual fluctuations). Analogous changes were observed in the 3d group.

Histochemical analysis of oxidative enzymes enabled us to demonstrate changes in oxidative metabolism. However, it was difficult to evaluate the efficacy of electrostimulation.

Electron microscopy indicated that, in the presence of hypokinesia, there were marked structural changes in the contractile system of muscle fibers, as manifested by separation of myofibrils, local lysis thereof, thickening and destruction of the stria.

With delivery of electrostimulation, there was variegation [mosaicism] of muscle fiber ultrastructure, size and shape of mitochondria, density of cristal packing, with appearance of many ribosomes and a large amount of glycogen. Some fibers presented necrotic areas.

The circumference of leg muscles, measured with a steel dynamometric tape, was diminished: by 13% in the 1st group, 5.5% in the 2d and 6.6% in the 3d.

Table 1. Cross section area, relative units, of muscle fibers

Conditions	Subjects	Red muscle fibers			White muscle fibers		
		before experiment	after experiment	change in fiber area, %	before experiment	after experiment	change in fiber area, %
Control group, hypokinesia	Ts-ich	33,3±0,9	22,7±0,6*	-33%	43,3±1,2	33,9±0,1*	-22%
Exercise after electrostimulation	Sh-ov	30,4±1,2	18,2±0,6*	-40%	42,1±1,3	23,4±0,6*	-45%
	S-in	26,04±0,9	23,5±0,3*	-10%	38,04±1,02	24,3±0,9*	-38%
Exercise before electrostimulation	Zh-v	18,7±0,5	23,7±0,9*	+27%	36,5±1,04	30,3±1,2*	-18%
	M-v	22,7±0,5	24,5±1,04	+8%	30,3±1,1	34,6±2*	+14%
	G-v	20,4±0,6	17,0±0,48*	-17%	27,02±0,7	26,0±0,9	-4%
	T-v	22,8±0,9	33,8±0,1*	+50%	33,6±0,7	38,9±1,3*	+10%
	K-n	21,7±1,2	29,4±0,9*	+35%	35,3±0,1	42,2±1,4*	+11%
	Su-n	24,1±0,5	27,5±1,0*	+14%	35,9±0,9	38,8±1,01**	+8%

Note: Asterisks indicate reliable differences, as compared to background values: *P<0.01 **P<0.05

Table 2. Indices of physical fitness [efficiency] before and after second experiment

Conditions	Sub-jects	Pedaling time on ergometer (min)			Maximum PR		Maximum O ₂ consumption, liters/min		Maximum O ₂ consumption, ml/kg/min	
		BG	RP, days	25	BG	RP, days	BG	RP, days	BG	RP, days
Control, hypokinesia	Ts-ch	8,20	5,00	4,05	182	180	2,4	2,24	33,5	31,5
	S-n	7,04	4,05	4,15	200	208	2,2	2,15	35,22	32,5
Exercise after ES	Sh-v	7,00	7,00	3,00	182	188	2,74	2,32	37,4	32,2
	M-v	9,45	9,42	10,00	188	190	2,72	3,34	37,2	45,7
	G-v	7,06	8,20	—	174	176	2,19	—	28,8	—
	Zh-v	8,40	8,40	8,00	184	182	2,64	3,06	37,5	43,4
Exercise before ES	T-v	7,27	9,05	8,40	188	188	2,51	2,76	35,3	39,4
	S-in	9,59	10,30	9,00	192	195	2,75	2,83	39,7	40,4
	K-n	8,52	9,15	7,40	180	178	2,46	2,59	33,2	37,8

Key: RP) recovery period

PR) pulse rate

BG) background

A study of static endurance of leg muscles revealed that this index declined by 9.9% in the 1st group and rose in the 2d and 3d groups by 51.6 and 36.2%, respectively.

In all three groups, there was a significant decrease in volume of work performed on the ergometer: by 36% in the 1st group, 30.7% in the 2d and 34.8% in the 3d.

Thus, there was approximately the same degree of reduction in volume of work performed in all of the groups.

In spite of the decreased volume of work, the rhythm of cardiac contractions was considerably faster than in the background period at the time the exercise ended, which is indicative of signs of deconditioning of the cardiovascular system. We failed to demonstrate appreciable differences between ES-20 and ES-12, with regard to effectiveness of stimulation.

Second series of studies: As in the first series, after completing the second one, there was reliable and significant reduction of cross-section area of red and white muscle fibers in the first group.

In all subjects who exercised before electrostimulation there was a reliable increase in cross section of red and white muscle fibers, but it was more marked in the red fibers.

In most subjects, who exercised after electrostimulation, there was an increase in cross section of red muscle fibers, with individual fluctuations in the direction of both increase and decrease in area of white fibers (Table 1).

The tests on the bicycle ergometer revealed that there was a significant decrease of efficiency in the 1st group: on the average, they pedaled 2 min less than before the experiment.

In the group that exercised after electrostimulation, efficiency remained at the original level, while in the group that exercised before electrostimulation it extended by an average of 1 min.

There was negligible change in heart rate at the time the subjects stopped pedaling on the ergometer, i.e., there was approximately the same "strain" on the cardiovascular system of subjects in all groups.

Maximum oxygen consumption increased in all groups of subjects who exercised (by a mean of 0.21 liter/min or 8%), while it decreased in the control group (by a mean of 0.32 liter/min, or 13%). When converted per unit body weight, maximum oxygen consumption increased in all subjects who exercised (by a mean of 3.6 ml/kg/min, or 10%) and in the control group it decreased by 4.3 ml/kg, or 12% (Table 2). This shows that in the conditioned subjects, the level of the cardiopulmonary system was completely retained. At the same time, it was higher in the group who exercised before electrostimulation; in the control group this level declined significantly. There was significant increase

in static endurance of subjects exposed to electrostimulation, combined with physical exercise, and decrease in the control group of subjects. However, the strength of postural muscles, as determined by a dynamometer, diminished in both the first and second experiment in all subjects, since the dorsal muscles were not involved in work and electrostimulation was not sufficient to preserve their strength.

What are the prospects of muscular electrostimulation as a means of preventing the disorders related to prolonged weightlessness?

To answer this, we must have a conception about the nature of muscular contractions during electrostimulation. They are intermittent and static, each contraction lasts 4 s and there are 2-s periods of relaxation between contractions. Each modulation of electric impulses presents gradual elevation and decline. Electrostimulation could be compared to isometric exercises which, by augmenting the strength indices of muscles, do not prevent deconditioning of the cardiovascular system [3].

Studies [1, 2] have shown that physical endurance exercises are an effective means of preventing deconditioning of the cardiovascular system under hypokinetic conditions.

It has been found possible to prevent muscular atrophy by means of electrostimulation thereof (in the first experiment); however, we did not succeed in preventing deconditioning of the cardiovascular system.

Endurance training (second experiment), combined with electrostimulation, elicited a distinct preventive effect. However, analogous results had been obtained previously [1] using only physical exercise, without electrostimulation. This shows the desirability of using physical endurance training in space flights as the main preventive measure.

Evaluation of effectiveness of electrostimulation of muscles using the Tonus-2 instrument should be investigated further.

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541/;35]-06:612.766.1/2

EXPERIMENTAL EVALUATION OF RELATIONSHIP BETWEEN PULMONARY BLOOD FLOW,
FLUID-ELECTROLYTE METABOLISM AND ORTHOSTATIC REACTIONS OF MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 68-74

[Article by I. D. Pestov, Kh. Kh. Asanov, B. F. Asyamolov, V. A. Karpusheva,
I. I. Kas'yan, V. S. Panchenko and V. I. Stepantsov, submitted 13 Feb 75]

[Text] In spite of the broad recognition of the mechanism of regulating fluid-electrolyte [salt] metabolism, known as the Henry-Gauer reflex, there is still no direct evidence of a link between quantitative indices of filling of volumoreceptor zones with blood and magnitude of fluid loss in man. Determination of blood volume in pulmonary capillaries, in studies involving the broadest possible range of influences on blood distribution in relation to the long axis of the human body, may be a means of demonstrating such a link. And, although the capillary network is not, in this instance, identified with the reflexogenic zone, by altering its supply of blood we could consider filling of the entire pulmonary circulation, including its volumoreceptor regions, a reliable enough indicator. A comparison of these data, indices of fluid-electrolyte metabolism and orthostatic reactions is important from the standpoint of objective evaluation of cause and effect correlations between these changes. Furthermore, such a study would permit evaluation of the extent of efficacy of preventive measures, presently used in space flights, with reference to all the indices mentioned and thereby broaden our conceptions of the mechanisms of their effects on the organism. This is all the more important, since there has not yet been sufficient physiological substantiation of some of the measures (for example, weighted suits).

Since there is relatively rapid formation of reactions related to changes in distribution of blood, we deemed it possible to limit ourselves in this study to a short experiment.

Methods

A series of tests (see Table) was conducted on 3 men 20-22 years of age; each test lasted 4.5 hours and the tests were performed once a week. The order of the experiments varied in each subject.

Characteristics of main and additional experimental tests

Additional tests						
Main test, 4.5 h	LBEP		LBNP		static axial load on body (TNK-2) 25 min × 7	
	no	+25 mm Hg,	25 min×7	-25 mm Hg,		25 min×7
	add.	5 min		5 min		
	tests	+35 mm Hg,		-35 mm Hg,		
		5 min		5 min		
		+40 mm Hg,		-40 mm Hg,		
		5 min		5 min		
	+30 mm Hg,	-30 mm Hg,				
	10 min	10 min				
15-min intervals between tests						
1% water load 2 ^h 55 ^m after start of test						
Sitting	I-1	I-2	I-3	I-4		
Lying down	II-1	II-2	II-3	II-4		
Antiortho- static position	III-1	III-2	III-3	III-4		

On the morning of the test, after 8 hours of sleep, the subjects relieved themselves, had breakfast (sour milk products, meat with garnish, glass of sweetened tea, bread, butter), and 1.5 hours after this meal, just prior to the test, they emptied their bladder and were weighed.

Hydrostatic blood pressure, in relation to the long axis of the body was maintained, removed and inverted (in series I, II and III of tests, respectively) in three standard positions (sitting in an armchair, lying in horizontal and antiorthostatic position, with the head of the bed tipped down at a 6° angle). Four tests were made in each of these positions (1st-4th groups). In control studies (1st group) the above hydrostatic conditions were not changed in any way. In the 2d group, we used excess pressure on the lower half of the body (LBEP) which ejected blood from the lower half to the upper. In the 3d group, we used negative pressure on the lower half of the body (LBNP), which diverted blood from the top to the bottom half of the body. In the 4th group, we created an axial static load on the body, the effect of which on distribution of blood was not known.

The LBEP and LBNP modes consisted of seven sessions with alternation of four pressure levels, the magnitude of which was the same in these tests, but the signs were different (see Table). To create LBEP, we used modified PPK-1-U (SPPK) anti-G suits, and for LBNP, a revolving chair with

an airtight [vacuum] section for the lower half of the body [2]. An axial load was delivered to the long axis of the body by using the adjustment system of a TNK-2 weighted suit [4], and it was kept constant (50 kg) throughout each of the 7 cycles.

In order to augment the information gained from short-term studies and, in particular, for more distinct demonstration of changes in fluid-electrolyte metabolism under different experimental conditions, we studied the rate of elimination of a 1% water load, which was delivered 2^h55^m after the start of the hypokinetic period. Fluid-electrolyte metabolism was monitored by determining the volumes, specific gravity, sodium composition of urine samples collected before, during and after the tests.

During the experimental period, we also kept a record of fluid intake due to the water load and changes in body weight. We estimated extrarenal loss and fluid balance.

Estimation of fluid balance did not include fluid and metabolic water contained in the morning meal, as a result of which there was a minor shift of the established indices in the direction of a negative balance, which was constant in all series.

We assessed the influence of experimental conditions on endurance of the vertical position by means of 5-min active orthostatic tests before hypokinesia (OS-1), 2.5 h after the start of hypokinesia before the water load (OS-2), 40, 80 and 120 min after the water load (OS-3, 4 and 4). We recorded the pulse rate during the orthostatic tests. In the course of the studies, we examined pulmonary diffusion with reference to carbon dioxide when breathing air and oxygen, as well as blood volume of pulmonary capillaries: before the test, in vertical and horizontal positions; during the test, in standard positions and with additional tests 1^h40^m, 3 h and 4^h15^m after starting the study.

The small number of subjects in the group did not enable us to make extensive use of mathematical statistical methods to analyze the experimental data. However, whenever we were able to classify the data according to some dominant feature, they were submitted to statistical processing.

Results and Discussion

Analysis of the results should be discussed starting with the general patterns that were inherent in the main experimental conditions.

Thus, the change from seated to horizontal and antiorthostatic position was associated, on the average for the 1st-4th groups (Figure 1), with an increased excretion of urine before the water load (U before WL) and over the entire period of the study (U₃), i.e., in 2.5 and 4.5 h, respectively. There was an increased rate of excretion of the water load in 80 and 120 min (% WL_{80,120}), as well as loss of potassium and sodium (K₁, Na₁), and negative fluid balance (F/B). There was an increase in blood volume of pulmonary

capillaries (V_a^k), absolute level and increment of pulse rate as the mean for 2-5 orthostatic tests (PR_{oc} 2-5, ΔPR_{oc} 2-5). In most cases, the indices in antiorthostatic position were reliably different from those in seated position. In other words, the increase in blood volume in the pulmonary circulation (V_a^k) stimulated loss of fluid and electrolytes, and for this reason lowered orthostatic resistance.

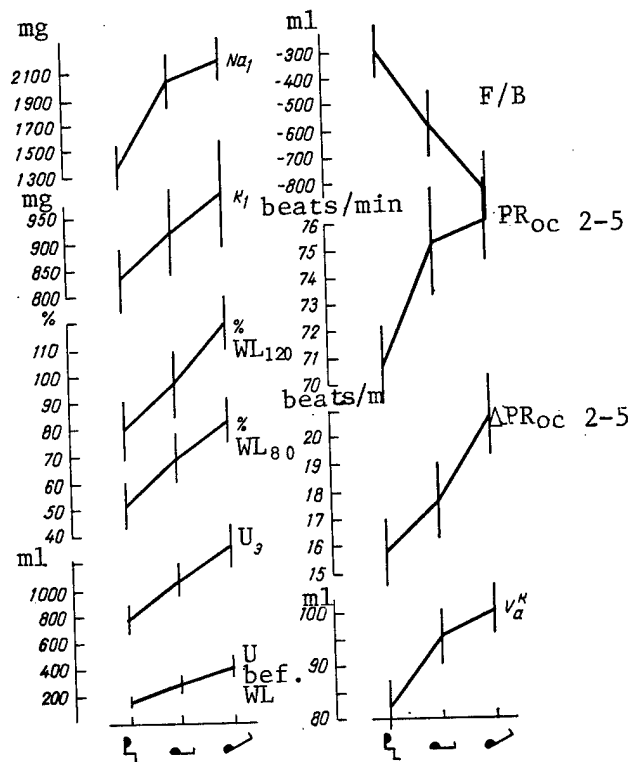


Figure 1. Mean (for 1st-4th groups) values of physiological indices in seated, horizontal and antiorthostatic positions. Explanation is given in the text.

Figure 2 illustrates the relationship between mean indices of filling of pulmonary capillaries and diuresis in the experiments. The capillary blood volume was in the range of 66-104.5 ml, while volume of urine over the entire study (with consideration of elimination of water load in 2 h) was 320-1570 ml. Since the same subjects participated in all of the series, the nature of relationship between two indices could be considered to be related solely to the test conditions. The direct, rather close and reliable correlation indicates that, in the case of short-term factors, there is a stable cause and effect relationship between flow in the pulmonary circulation and diuresis, which is the basis of the Henry-Gauer reflex. Under the specific conditions of our study, each 10 ml change in filling of pulmonary capillaries altered diuresis by an average of 1.2 ml/min.

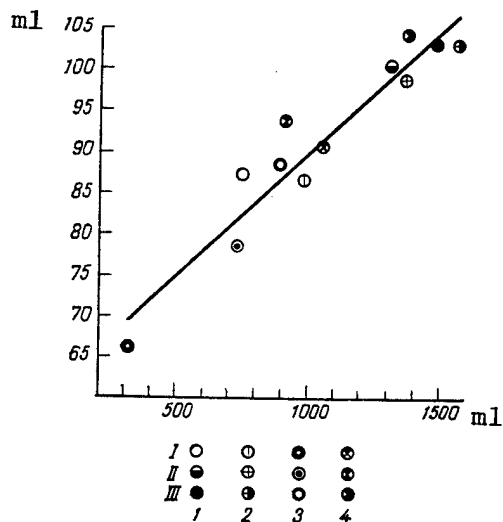


Figure 2.
Link between mean group indices of
filling of pulmonary capillaries and
diuresis; x-axis, urine volume over
experimental period, ml; y-axis, blood
volume in pulmonary capillaries, ml
 $r = 0.954$; $P < 0.001$

These studies also enable us to give more details concerning the above-mentioned view (see Figure 1) concerning a link between fluid loss and orthostatic changes. Examination of Figure 3, where such a comparison can be drawn for all of the studies, makes it clear that this link is demonstrable with utmost clarity in the control group of experiments (1st group). The additional tests used with the subjects in different positions, in the 2d-4th groups, sometimes distorted the nature of this link, as manifested by disproportionate change in fluid metabolism and orthostatic stability. Since it is imperative to comprehend the mechanisms of this modifying influence to set proper standards for preventive measures, this question merits closer scrutiny. It was found that expulsion of blood from the vessels of the lower half of the body to those of the upper half, as a result of using LBEP in seated position (series I-2) increased fluid loss in urine, rate of excretion of water load, negative fluid balance and orthostatic changes in pulse rate, as compared to control series I-1. Conversely, diversion of blood from the upper half of the body to the lower, by means of LBNP, diminished appreciable the changes in fluid metabolism and orthostatic stability, as compared to series II-1 and III-1, in horizontal and antiorthostatic positions. It should be noted that, in these situations, the effects of LBEP and LBNP did not coincide with the influence of natural hydrostatic pressure. The findings were different in the experimental series where the additional physical factor had an effect that coincided with that of hydrostatic blood pressure. Thus, in horizontal and antiorthostatic positions, the effect of LBEP was, as before, manifested by some increase in changes in fluid metabolism, but in this instance the orthostatic changes diminished, as compared to control series II-1 and III-1. In seated position, LBNP in seated position blocked extremely effectively a change in fluid metabolism, but worsened orthostatic stability, as compared to control series I-1. In all probability, involvement of some additional factor, which went into action under the concomitant effect of hydrostatic pressure, on the one hand,

and LBNP or LBEP, on the other, was the cause of disproportion between changes in fluid metabolism and orthostatic stability.

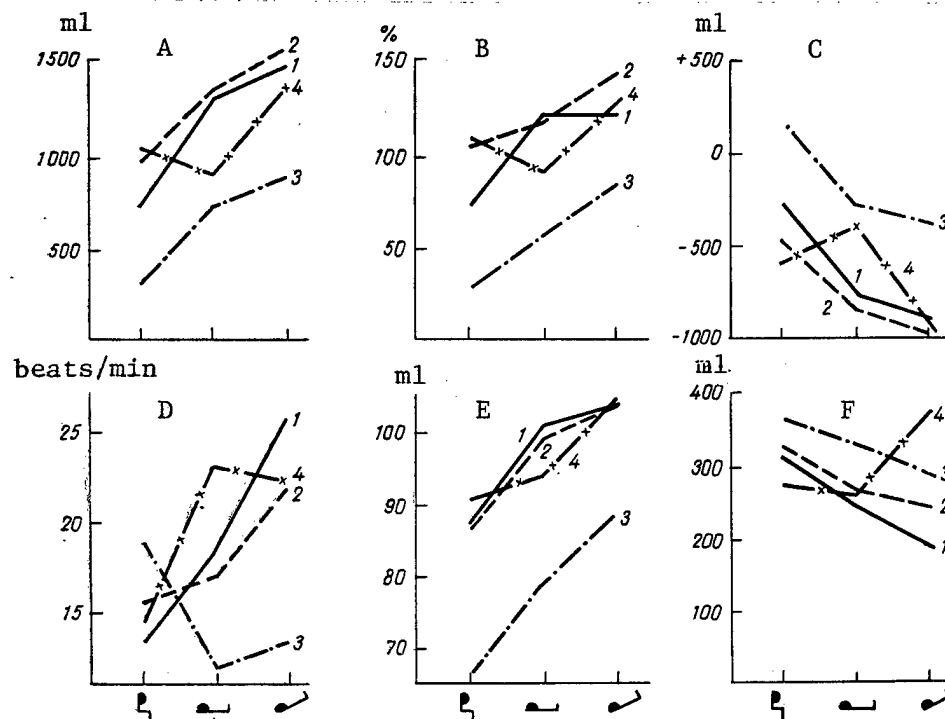


Figure 3. Physiological indices as related to different positions in groups 1-4

- | | |
|--|-------------------------------------|
| A) volume of urine over experiment, ml | D) pulse rate increase, per min |
| B) elimination of water load in 2 h, % | E) blood volume in lung capill., ml |
| C) fluid balance, ml | F) extrarenal fluid loss, ml |

The experience gained in previous investigations [1, 3] warrants the assumption that elasticity of vessels in the lower half of the body could be such an additional factor. The lower hydrostatic pressure in these vessels, along with the effect of LBEP, could cause a decrease in elasticity due to residual deformation (hysteresis), which is advantageous, from the standpoint of endurance of orthostatic factors. Conversely, the effect of natural hydrostatic pressure in seated position, combined with LBNP, could lead to increased stretching of vessels of the lower limbs and capacity of venous pool in the lower half of the body, which worsens tolerance of vertical position. Of course, this working hypothesis, which explains the paradoxical discrepancy between the state of fluid metabolism and orthostatic stability, requires direct experimental verification.

As we see from the results obtained in the 4th group, an axial static load over the long axis of the body also modifies the reaction with reference to

fluid metabolism and orthostatic stability, as compared to the first group. However, it is difficult to qualify the nature of this modifying effect without pursuing additional studies. We were impressed by the fact that, in horizontal position, there was a disproportionate relationship between changes in fluid metabolism and orthostatic stability.

Thus, these studies confirmed and defined the quantitative correlation between delivery of blood to the pulmonary circulation and regulation of fluid-electrolyte metabolism, which is the basis of the Henry-Gauer reflex. We also obtained facts indicative of disproportionate correlations between changes in fluid metabolism and orthostatic stability. From the practical point of view, the latter means that an overdose of LBNP could have an undesirable effect on orthostatic stability, in spite of the fact that, in this instance, fluid metabolism would be normalized. Although this situation occurred in the experiment only with the subjects in seated position, under the influence of stronger LBNP it could also appear in other positions and, consequently, in weightlessness. The higher orthostatic stability in the series where LBEP was used in horizontal and antiorthostatic positions, as compared to the control, leads us to the paradoxical conclusion that it would be expedient to use such a measure, not only in the postflight period, as is currently done, but in the course of a space flight. However, this conclusion requires broader and more comprehensive substantiation. We are not quite clear as to the consequences of an axial static load on distribution of blood, fluid metabolism and orthostatic stability in a laboratory simulation of weightlessness, and this also requires further research.

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SENSITIVITY OF HYPOKINETIC ANIMALS TO CENTRAL NERVOUS SYSTEM STIMULANTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 74-79

[Article by L. Ya. Kolemeyeva, V. S. Shashkov and B. B. Yegorov, submitted
25 Feb 75]

[Text] The opinion has been voiced in works by Soviet and foreign authors
that it would be desirable to include nervous system stimulants in on-
board medicine kits [1, 8, 9].

However, in the literature available to us, there are only a few publica-
tions reporting on the effects of stimulants taken by individuals who had
maintained bedrest for long periods of time [2-3].

At the same time, it is of definite theoretical and practical interest to
investigate sensitivity of animals to such agents, when given separately
under conditions of restricted motor activity (RMA).

The present work was pursued to investigate the effects of RMA varying in
duration on animal sensitivity to central nervous system (CNS) stimulants.
We selected for this study stimulants with a predominant effect on different
parts of the CNS. These agents were also used as pharmacological analyzers
of impairment of physiological functions associated with RMA.

Methods

Experiments were conducted on 1150 white, mongrel male rats weighing 200 ± 50 g.
The experimental animals were kept in cages that restricted mobility for 1,
5, 10, 15, 30, 45 and 60 days. Control rats were not subject to such
restriction. The animals were fed a standard diet. CNS stimulants--caffeine,
phenamine [amphetamine] and strychnine--were injected intraperitoneally
after the above-listed RMA periods.

In order to determine LD_{16} , LD_{50} and LD_{84} , the agents were given in the
following doses: 540, 600, 660, 700 and 760 mg/kg caffeine; 25, 35, 45, 55
and 65 mg/kg phenamine; 2.5, 3.0, 4.0 and 4.5 mg/kg strychnine.

At the beginning of the experiment, we determined LD₁₆, LD₅₀ and LD₈₄ according to survival of intact rats (absolute control). In both the absolute control and experiment, each dosage was tested on eight rats. In addition to the absolute control, we ran an additional control for LD₅₀ at each stage of hypokinesia.

We used the following criteria to evaluate changes in sensitivity of the organism to CNS stimulants: 1) quantitative changes in LD₁₆, LD₅₀ and LD₈₄ of all agents tested for experimental animals, as compared to the control; 2) time of appearance and duration of following behavioral reactions: adynamia (caffeine), "stereotype" behavior (phenamine) and seizures (strychnine).

Since, according to the tests used, the changes in sensitivity to CNS stimulants were identical in both the absolute control and parallel tests at each stage of hypokinesia, we have submitted in the figures and Table changes compared to the absolute control.

The LD₁₆, LD₅₀ and LD₈₄ were calculated by the least squares method [10], and the other indices were submitted to processing by the method of variation statistics according to Student-Fisher [4].

Results and Discussion

As can be seen in the Table, sensitivity to CNS stimulants was related to both duration of RMA and spectrum of action of the agent tested.

With administration of caffeine, we observed increases in sensitivity of experimental rats, according to all three LD on the 5th, 30th, 45th and 60th days of RMA by an average of 24, 15, 25 and 10%, respectively ($P < 0.001$, < 0.02 , < 0.01 and < 0.05 , respectively). There was little difference between experimental and control rats, with regard to sensitivity to caffeine after 1 and 10 days of RMA. Maximum decrease in resistance to this agent was observed in experimental animals after the 15th day of RMA, according to LD₁₆ (35%, $P < 0.001$).

In our opinion, of greatest interest was the reaction to phenamine, an agent whose mechanism of action is closely related to metabolism of biogenous amines (see Table). We observed phasic changes in sensitivity of experimental rats with regard to all three LD. For the first 10-12 days of RMA, we observed heightened sensitivity to phenamine, then a decline up to the 35th-40th day of RMA, then another increase in sensitivity to the end of the experiment, by 71.6% ($P < 0.001$) for LD₁₆, 37.7% ($P < 0.001$) for LD₅₀ and 20.6% ($P < 0.01$) for LD₈₄.

With administration of strychnine, we observed significant increase in reactivity of the organism after 5 and 45 days of RMA with reference to LD₁₆ (by 40.0%; $P < 0.001$), whereas sensitivity increased only on the 45th day, by 35% ($P < 0.001$) according to LD₅₀.

Changes in sensitivity of hypokinetic animals to CNS stimulants

Agent	Toxic dosage	Absolute control	Days of hypokinesia						
			1	5	10	15	30	45	60
Caffeine	LD ₁₆	488.5 (100)	490.0 (100.3)	352.2* (72.1)	497.5 (101.8)	317.1* (64.9)	407.4* (83.4)	350.7* (71.8)	448.0 (91.7)
	LD ₅₀	642.4±36.8 (100)	615.0±29.1 (94.3)	1497.1±42.0 (76.2)*	622.5±31.6 (95.4)	602.8±64.9 (85.3)*	556.7±34.3 (83.8)*	492.7±42.0 (75.5)*	581.3±29.9 (89.1)*
	LD ₈₄	816.5 (100)	740.0* (90.6)	642.0* (78.6)	747.5 (91.5)	888.5 (108.8)	705.9* (86.4)	640.6* (78.4)	714.7* (87.5)
	LD ₁₆	30.3 (100)	27.8 (91.7)	24.2* (79.9)	7.8* (25.7)	30.9 (101.9)	43.5* (143.5)	22.2* (73.3)	8.6* (28.4)
Phenamine	LD ₈₄	44.8±3.6 (100)	46.3±4.2 (103.3)	37.0±2.9* (82.6)	32.2±5.5* (71.8)	46.6±3.5 (104.2)	55.7±3.0* (124.3)	33.2±2.9* (74.1)	27.9±5.0* (62.3)
	LD ₅₀	59.3 (100)	64.8 (109.3)	49.9 (84.1)	56.6 (95.4)	62.2 (104.8)	67.9* (114.5)	44.2* (74.5)	47.1* (79.4)
Strychnine	LD ₁₆	2.00 (100)	1.61* (80.5)	1.19* (59.5)	1.90 (95.0)	1.70* (85.0)	1.80* (90.0)	1.18* (59.0)	1.52* (76.0)
	LD ₃₀	3.16±0.26 (100)	3.00±0.31 (94.9)	3.16±0.33 (100.0)	3.47±0.37 (109.8)	2.93±0.31 (92.7)	2.96±0.26 (93.7)	2.06±0.37 (65.2)*	2.97±0.33 (93.9)
	LD ₈₄	4.32 (100)	4.39 (100.1)	4.14 (95.8)	5.03* (111.6)	4.15 (96.1)	4.13 (95.6)	4.12 (95.4)	4.42 (102.3)

Note: Figures in parentheses refer to percentage in control. Asterisks refer to statistically reliable results.

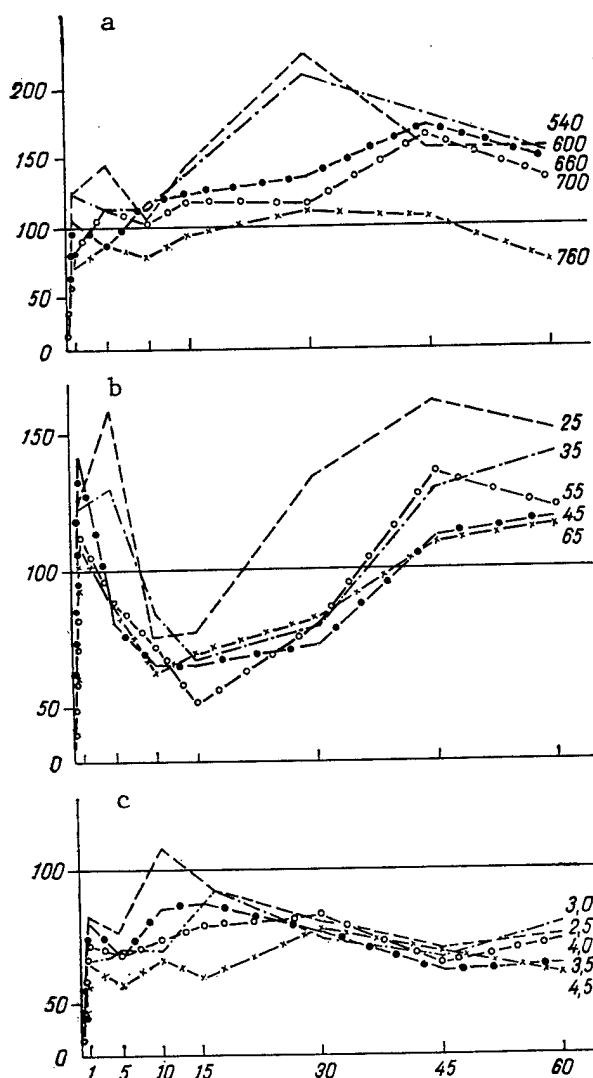


Figure 1.

Time (s) of appearance of behavioral reactions in rats given CNS stimulants (in mg/kg) following different periods of hypokinesia; y-axis, time of appearance of behavioral reactions (% of control taken as 100%)

X-axis, days of hypokinesia

a) caffeine

b) phenamine

c) strychnine

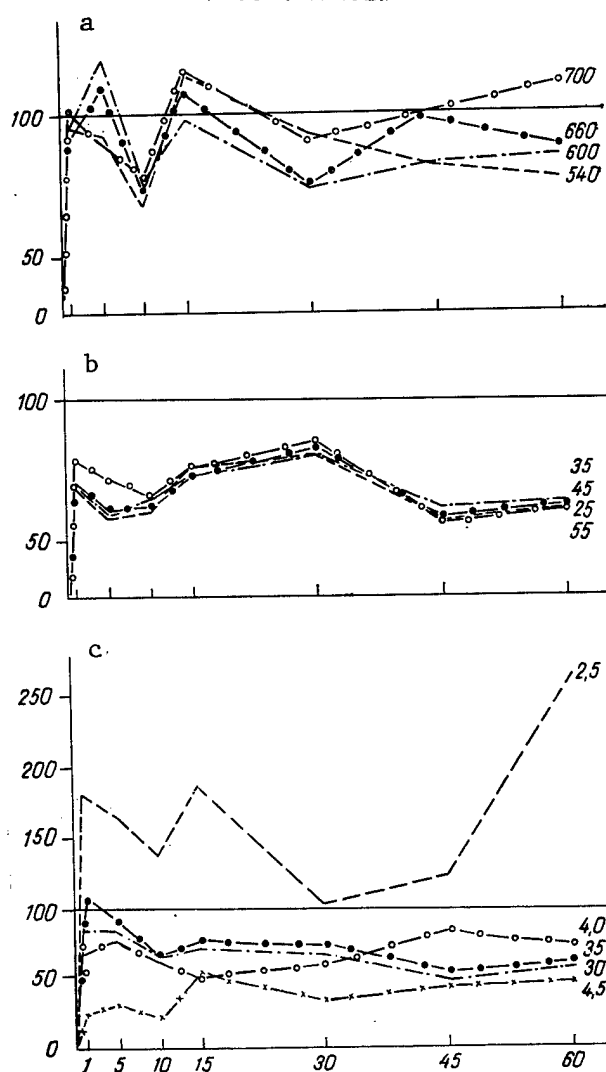


Figure 2.

Duration of adynamia, "stereotype" behavior (min) and seizures (s) in hypokinetic rats after administration of caffeine, phenamine and strychnine (mg/kg); y-axis, duration of behavioral reactions (% of control taken as 100%)

The behavioral reactions of experimental animals differed from those of the control. Thus, with administration of caffeine, in doses of 540, 600, 660 and 700 mg/kg, we observed later onset of adynamia in experimental animals starting on the 15th day of RMA and to the end of the experiment. Maximum changes were noted on the 30th day of RMA with administration of 540 and 600 mg/kg caffeine. Thus, with 540 mg/kg caffeine, adynamia occurred 290.6 s later in experimental animals and 138.1 s later in controls ($P < 0.001$); with 600 mg/kg, adynamia was observed in experimental rats after 326.7 s and in controls, after 144.6 s ($P < 0.002$). Reliable changes in onset of adynamia were also noted after 45 and 60 days of RMA, with administration of the above-mentioned doses of caffeine. When caffeine was given in a dosage of 760 mg/kg, we observed earlier onset of adynamia in experimental animals after 1, 10 and 60 days of RMA (after 131.2, 145.6 and 138.88 s in the experimental animals and 186.2 s in the control; $P < 0.001$, < 0.01 and < 0.001 , respectively). At other periods of RMA, time of appearance of adynamia in experimental animals was similar to that observed in control rats (Figure 1a). Duration of adynamia fluctuated in experimental animals (Figure 2a). The most reliable changes after administration of all tested doses of caffeine were observed after 10 days of RMA. With doses of 540 and 600 mg/kg caffeine, reliable changes were noted after 30, 45 and 60 days of RMA: adynamia lasted less time in experimental animals than controls.

With administration of phenamine, there were phasic changes with regard to time of onset of "stereotype" behavior in experimental animals (Figure 1b). Thus, with all 5 doses, reliable changes in time of occurrence of "stereotype" behavior were noted after 10, 15, 45 and 60 days of RMA.

In all periods of RMA, "stereotype" behavior lasted for a shorter time in experimental animals than in the control (Figure 2b).

With administration of strychnine, seizures occurred sooner in experimental animals. The only exception was a dosage of 2.5 mg/kg, after which seizures occurred later in experimental animals, after 10 days of RMA, but these data are unreliable (see Figure 1c). Reliable changes with administration of all 5 doses of strychnine were observed only after 45-60 days of RMA.

The seizures lasted for a shorter time with large doses of strychnine (3.0-4.5 mg/kg) than in controls, whereas with administration of small doses of strychnine (2.5 mg/kg) their duration increased in experimental animals. Reliable changes were demonstrable only after 60 days of RMA (Figure 2c).

Thus, on the basis of quantitative estimation of LD_{16} , LD_{50} and LD_{84} , we can detect a phasic nature in the change in sensitivity to CNS stimulants as function of duration of RMA. Maximum phasic changes in sensitivity were noted with administration of phenamine. An appreciable increase in sensitivity to caffeine was demonstrated on the 5th, 15th and 45th days of RMA, and to strychnine only on the 5th and 45th days.

Our data concerning changes in behavioral reactions of experimental animals revealed that seizures after giving strychnine occurred sooner than in

controls, and their duration was related to doses given. Thus, with large doses of strychnine (3.0-4.5 mg/kg) the seizures were briefer and with a small dose (2.5 mg/kg) they lasted longer.

Adynamia occurred later in experimental animals after intake of caffeine, on the 15th day of RMA, while duration thereof fluctuated.

With administration of phenamine, we observed phasic onset of "stereotype" behavior in experimental animals and it lasted for a shorter time than in the control.

It had previously been demonstrated, on the example of narcotic agents, that there are phasic changes in sensitivity of the animal organism, against the background of RMA, to narcotics referable to different classes of chemical compounds [6, 7]. The hypothesis had been voiced that impairment of functional correlations between excitatory and inhibitory processes in the CNS, in the direction of more excitatory processes, was the chief cause of lower sensitivity of the organism to narcotics. The increased sensitivity of hypokinetic animals to CNS stimulants confirms this hypothesis.

Perhaps, the increase in excitatory processes in the CNS in the presence of hypokinesia is due to increased catabolism of biogenous amines, in particular serotonin [5]. Analogous changes in concentration of serotonin have been demonstrated as well in animals following space flights [11].

In spite of the fact that agents of the phenamine class are the most potent and reliable stimulants of physical and mental efficiency, inclusion thereof in onboard medicine kits should be recommended only for intake one time, in emergency cases of critical situations. It is impossible to regularly prescribe phenamine and its analogues as stimulants of primarily mental, rather than physical efficiency. In this case, preference should be given to caffeine, and in the case of severe asthenization of the organism, one can prescribe strychnine as a system tonic agent.

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INVESTIGATION OF MECHANICAL ACTIVITY OF CANINE SKELETAL MUSCLES IN VIVO

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 79-83

[Article by V. G. Kozlova, V. S. Oganov and A. S. Rakhmanov, submitted
8 Aug 75]

[Text] The search for direct methods of studying the mechanical activity of skeletal muscles is justified, not only by theoretical considerations, but by some of the applied problems of space physiology [2]. The results of manned space flights [1, 11], as well as model studies on man [3, 4, 6] and animals [5, 8], have shown, in particular, that it is desirable to record some parameters of muscular contractions under dynamic conditions, i.e., during the contraction proper, when studying the effects of different space flight factors on the locomotor system. A previously proposed [2] method of recording muscular exertion, dynamomyography, meets this goal. In this report, we offer a qualitative description of mechanical activity of different muscles of the dog, recorded by this method in different modes of locomotion, and preliminary analysis of some quantitative correlations between strength characteristics of muscles and their electrical activity.

Methods

The studies were conducted on 18 adult male dogs weighing 7-8 kg. We used a miniature implanted titanium transformer to record the dynamomyogram (DMG). The basic device and design of the transformer, surgical technique for long-term implantation thereof, as well as the method of recording muscle activity have been described comprehensively previously [7]. Surgery was performed under nembutal anesthesia to immobilize the transformer on an intact tendon of the gastrocnemius or plantar muscle. At the same time, steel electrodes (11 diameter, 5 mm length) were implanted 1.5-2 cm apart in the same muscle to record the electromyogram (EMG). The lead-off wires from the transformer and electrodes, which were passed under the animals' skin, were connected by means of the plug [unit?] part of a plug and socket unit (RS-10) on a fluoroplastic base that was immobilized, during the same operation, on the skin of the dorsal surface of the neck. The external part of the lead-off wires from the plug and socket unit were so arranged as

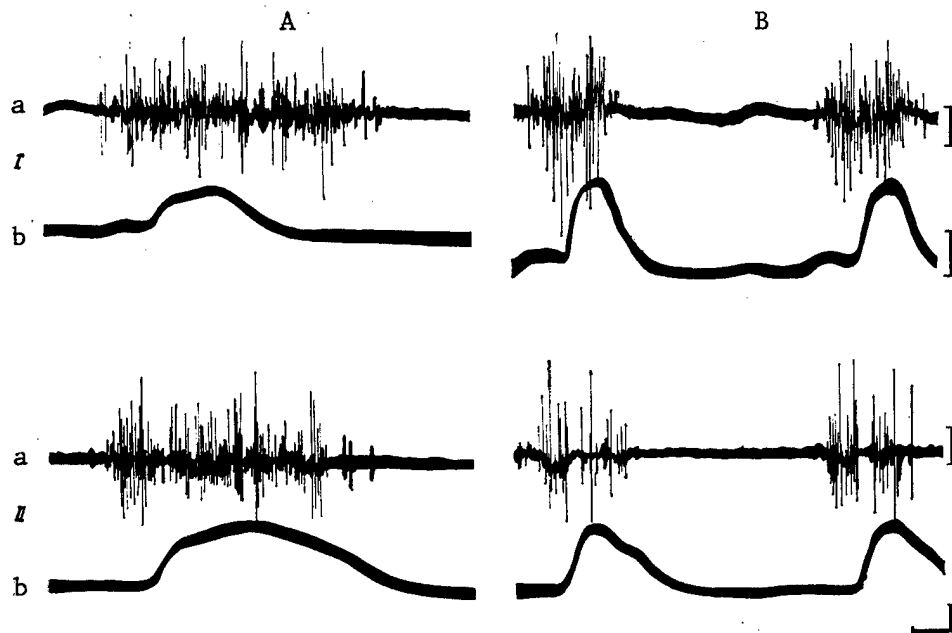
to allow the animals freedom in moving on a treadmill, which moved at the rate of 0.5 and 1.2 m/s. Under the conditions, locomotion was arbitrarily classified as walking and running, respectively. The variables studied were recorded on a nonstandard, multichannel magnetic recording device with a maximum frequency of 1 kHz. The data were processed using an MN-10 analog computer, ATAS-401 computer and M-220 electronic computer.

Results and Discussion

The Figure illustrates the DMG of the dog's gastrocnemius and plantaris while walking and running, as compared to electrical activity. The DMG of the muscles studied are stable bursts of muscular exertion, the frequency of which coincides with the pace of locomotion. Qualitative analysis enabled us to demonstrate some differences in the overall pattern of the muscles in question. The curve reflecting one cycle of gastrocnemius exertion during walking rises rather rapidly then tapers down, resembling the shape of a bell. The slope of the DMG of the plantaris, in the linear segment, differs little from that of the gastrocnemius. However, rise of the exertion curve to a maximum covers a longer time and then, for some time, it holds at about the same level, so that on the whole the plantar DMG during walking approximates the shape of a trapeze. This analysis applies to the main wave of exertion, reflecting the direct development of tension in the muscle at the shock-absorbing phase in response to electrical stimulation. This wave presents some lag, in relation to the start of electrical activity, and it can apparently serve as an index of condition of the muscle during natural movements. At the same time, the DMG of the gastrocnemius, unlike the plantar muscle, showed an additional exertion wave, preceding the main one and arising virtually simultaneously with electrical activity (see Figure). Additional cyclogrammetric analysis of walking and running leads us to assume that this first wave may be a manifestation of the pseudostretch reflex [9].

The difference in shape of exertion curves of different muscles may be related to both their anatomical and morphological distinctions. The plantar muscle, together with the gastrocnemius, flexes the knee and extends the ankle joint. However, according to the studies of Bradley [10], the short flexor of phalanges, which flexes the 2d-5th phalanges and extends the ankle joint, is the direct continuation of plantar muscle tendon. Thus, the anatomotopographical distinctions of the plantar muscle could explain why it retains activity, being a synergist of the gastrocnemius, for a longer time during the same cycle of walking. At the same time, this could also be due to the more heterogeneous composition of plantar muscle fibers, as compared to the gastrocnemius.

Inertial factors acquire more significance when changing from walking to running, in the overall structure of the locomotion act, and the dynamomyograms of the muscles studied appear to lose differences. However, preliminary quantitative analysis enabled us to demonstrate additional differences between the muscles in each of the locomotion modes.



Electrical activity (a) and dynamomyogram (b) of the gastrocnemius (I) and plantar muscle (II) of a dog while walking (A) and running (B). Calibration: 500 μ V, 1 kg, 50 ms.

The following parameters were used for quantitative evaluation of mechanical activity and its correlation with electrical activity: maximum exertion developed by the muscle, as related to dog weight (F); latency period of mechanical activity, or electromechanical lag (t_e); duration of mechanical activity (T_F); time of development of maximum force (t_{FM}); area under the curve of mechanical activity (S).

As can be seen in the Table, in the absence of appreciable difference in latency period, the plantar muscle develops a greater force than the gastrocnemius in the same mode of locomotion, and particularly while walking.

Parameters of mechanical and electrical activity of muscles at different rates of locomotion

The duration of mechanical activity, as well as time at which maximum exertion of the plantar muscle is reached are reliable greater than these parameters in the gastrocnemius (by 20 and 266%). In accordance with these data, the area of mechanical activity of the plantar muscle is about 100% larger than the area of mechanical activity of the gastrocnemius. Thus, the quantitative description of walking confirms the differences demonstrated in the qualitative analysis, showing, for example, that in walking the plantar muscle performs more work than the gastrocnemius.

When the dog switches to running, there is shorter time of contact between the limb and base [6], and accordingly there is a change in time and force parameters of the muscles, manifested differently in the muscles studied. Thus, with a change in rate of locomotion from 0.5 to 1.2 m/s, the amplitude of exertion of the gastrocnemius increases by 93%, while that of the plantar muscle shows a 44% increment. This could be indicative of the hypothesis expounded, to the effect that the plantar muscle is more heterogeneous in composition of fibers. At the same time, no reliable difference was demonstrated in degree of reduction in time of mechanical activity of both muscles with the change from walking to running. Under the same conditions, the time required to reach maximum exertion diminishes from 165.0 ± 13.0 to 86.4 ± 6.0 ms, i.e., by 48%, for the plantar muscle. This parameter decreases by 12% for the gastrocnemius.

According to preliminary data, this is associated with a 30% decrease in area of mechanical activity of the plantar muscle with the change from walking to running. At the same time, the area under the curve of mechanical activity of the gastrocnemius shows no appreciable change. The lack of changes in area of mechanical activity of the gastrocnemius is due to a decrease in time parameters of muscle contraction and concurrent, significant increase in amplitude of exertion, as can be seen in the Table. At the same time, the more marked change in time parameters for the plantar muscle, in the absence of significant force increment, leads to a reduction in area under the mechanical activity curve of this muscle. As shown by the results of these studies, the gastrocnemius, the amount of work of which does not change with the transition from walking to running, is apparently the leading muscle of the hind leg in locomotion.

Thus, we are able to describe the qualitative distinctions of biomechanics of contraction of different muscles in the course of natural movement and to obtain quantitative characteristics of changes in different parameters of contraction of different muscles, as function of locomotion mode, by recording exertions in the course of isotonic contraction of muscles. Evidently, this makes it possible to record functional manifestations of anatomical and morphological distinctions of different muscles. Finally, the quantitative characteristics of force parameters of contraction of different synergistic muscles of the hind leg enable us to assess the extent of their participation in four-legged locomotion.

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METHODS

UDC: 615.47:612.76-087.5

A PORTABLE DEVICE FOR DETERMINING STATIC ENDURANCE OF RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 83-84

[Article by A. A. Shipov and A. S. Markin, submitted 19 Mar 76]

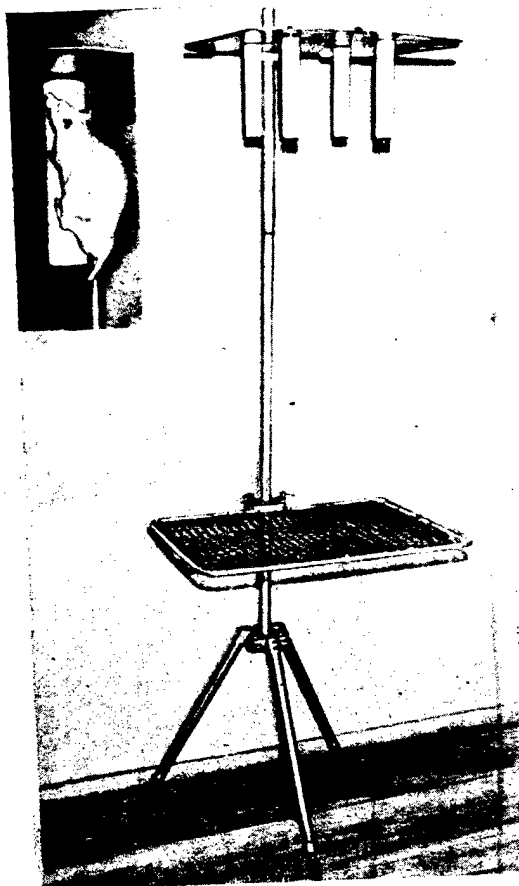
[Text] Studies of physical efficiency of animals [3] occupy an important place in applied physiology. Physical efficiency is usually evaluated by the degree of static and dynamic endurance. Static endurance of small laboratory animals (rats, mice) is determined by the time that an animal can hold on to a vertical screen, top or side surface (with notches or rubber rings) of a vertical pole 170-180 cm high [1-3]. "Electric prodders" [1] are used, or else the base of the pole is placed in cold water [2] to make the animal perform.

However, as shown by experiments on rats, physical factors alter the results of subsequent physiological studies, and they do not rule out the possibility of the animal actively jumping or sliding down the pole, which makes it difficult to measure the maximum time it can hold on and does not permit obtaining reliable data on its true endurance.

The objective of this study was to develop a method of determining static endurance of rats that would not have the above-mentioned disadvantages.

We decided to use the natural fear of heights as the only factor compelling the animal to perform static work. For this purpose, the animal was placed on the lateral surface of a short post, with a light platform on the top 170-180 cm above the floor. We found that, in this case, the structure and quality of the holding surface had a decisive effect on the animals' behavior on the pole. For example, if the poles consisted of aluminum tubes with rubber rings or a wooden rod with notches on them, the rats would actively move away from the surface of the poles and jump to the floor. Holding time, in this case, constituted a few seconds and, of course, could not serve as a gauge of static endurance. Only after we covered the entire pole with porolon was it possible to determine holding time. Shortly before the rats dropped to the floor, they usually held on to the tip of the pole with all four limbs, then the hind legs broke away from the pole, the

animals remained suspended for some time on their forelegs and, finally, fell to the floor. There was virtually no delay in the next fall, after the fallen rats were put back on the pole.



Device for studying
static endurance of rats.

Explanation is given in
the text.

On the basis of 100 experiments to develop the method, we designed a portable device for determination of static endurance of rats.

The device (see Figure) consists of several poles suspended vertically from a platform attached to a stand 180-200 cm high. The platform and poles can be used separately, in which case it is attached to a wall or any other vertical surface with a bracket.

The poles are made of aluminum tubing (2 cm in diameter, 18 cm long) and they are entirely coated with 1 cm porolon.

In the case of concurrent testing of several animals, there must be a distance of at least 20 cm between the tubes, and at least 12 cm between the tube and edge of the platform so that the animals could not climb from tube to tube or on top of the platform.

The animal falls on a support, which consists of a folding, 50×80 cm frame, with small-gage elastic screening stretched over it. This support is secured in horizontal position to the stand, at a height of 80-100 cm.

The device is light in weight (3-4 kg), it can be easily disassembled, and it is convenient for use in both the laboratory and in the field.

Determination of static endurance on the proposed device of over 500 male rats of different ages (Wistar, Wistar-SPF, mongrel) revealed that the maximum holding time is characterized by minor scatter and great stability in animals of the same weight.

It should be noted, that when the animals weigh less than 130 g, there is a sharp increase in holding time (1 h or more).

The above advantages of this device (lack of physical stimuli, minor scatter of obtained data, simple construction, small weight and portability) enable us to recommend it for wide use in studies related to changes in physical efficiency of animals under the influence of the most diverse factors.

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BRIEF REPORTS

UDC: 612.22-06:[612.766.2+612:273.2

DIFFUSION CAPACITY OF THE HUMAN LUNGS UNDER THE COMBINED EFFECT OF HYPOKINESIA AND HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 pp 85-86

[Article by A. N. Kotov, submitted 27 Feb 75]

[Text] Extensive work has been done in recent years to find the optimum gas environment for small sealed chambers [1, 10, 12].

Restricted mobility is the main pathogenetic factor in onset of hypokinetic disorders in man when he stays in such chambers for long periods of time [5, 11]. An "active" gas environment has been proposed as a preventive measure to control the sequelae of long-term hypokinesia [2, 10].

Extensive factual material has been accumulated to date on dynamics of lung diffusion (D_L) in the presence of functional and pathological changes in the respiratory and circulatory systems [3, 4, 6, 8].

We did not encounter, in the available literature, any works dealing with human D_L as related to restricted motor activity and use of altered gas environment as a means of preventing hypokinetic disorders.

The objective of this study was to demonstrate the mechanisms of changes in D_L of man in the presence of hypokinesia, as well as under the combined effect of hypokinesia and hypoxia.

Methods

These studies were conducted on two groups of males ranging in age from 25 to 35 years, who were kept on strict bed rest for 49 days. The first was a control group (10 people) and the second consisted of 3 men who breathed daily a gas mixture containing 13% O_2 in N_2 , twice a day for 3 h (from 0900 to 1200 hours and from 1600 to 1900 hours). D_L was determined by the steady state method using the Diffusiotest--Godart instrument. The subject alternately inhaled a mixture of air and CO (about 0.04% concentration of CO) and oxygen and CO (about 0.4% CO concentration). Determination was made of CO in inspired, mixed expired and alveolar air by means of an infrared

analyzer. The alveolar portion of exhaled air was obtained by means of the special sample collector of Rahn and Otis. Determination of D_L with different partial oxygen pressures permits determination of diffusion capacity of the membrane (D_M --membrane component) and amount of blood in pulmonary capillaries (V_C --capillary component). Calculations of D_L , D_M and V_C were made using the following formulas:

$$\frac{1}{D_L} = \frac{1}{D_M} + \frac{1}{\Theta V_C} \quad \& \quad D_L = \frac{[F_{in} - (F_{ex} - C_{ex})] \cdot MV}{(F_{et} - C_{et}) \cdot (P_b - 47)},$$

where Θ is the constant of rate of oxygen binding with hemoglobin; MV is minute volume of ventilation; P_b is barometric pressure; F_{in} , F_{ex} and F_{et} are concentrations of CO in inspired, expired and alveolar air, respectively; C_{ex} and C_{et} are deviations of CO before the test in exhaled and alveolar air.

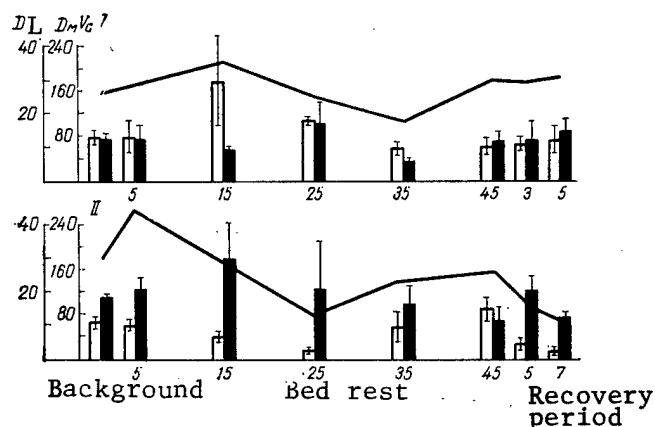
Studies of D_L were made in the background period, 5th, 15th 25th, 35th and 45th days of hypokinesia, and 3d, 5th and 7th days of the recovery period. Determination of D_L was made under basal metabolic conditions. The data were submitted to statistical processing by the method of Student.

Results and Discussion

The results of determining D_L are illustrated in the Figure.

The results are indicative of unidirectional phasic change in D_L in the two groups of subjects. It should be noted that, in the 2d group, increase in D_L and subsequent return to the initial level occurred on the average of 10 days sooner than in the control group. The initial distinct tendency toward increased diffusion in the 2d group is related to a change in V_C ($P > 0.05$), which remains high for the first 15 experimental days. By the 25th day of the study, we observed restoration of V_C to its initial level. Maximum resistance to diffusion through the alveolocapillary membrane ($P < 0.05$) was observed on the 25th day of the experiment. The initial value of D_M was restored on the 35th day. The predominant value of V_C in dynamics of D_L in the 2d group of subjects is due, in our opinion, to the stimulating effect of periodic respiration of a hypoxic gas mixture. For example, Forster et al. [9] observed an increase of D_L in individuals when there was a low PO_2 in inspired air. It is also known that, under hypoxic conditions, there is appreciable elevation of pressure in the pulmonary circulation. Thus, Kronenberg et al. [10] demonstrated elevated pressure in the pulmonary artery of 3 subjects with catheters implanted in the left pulmonary artery during a 72-hour stay at an altitude of 3800 m, in the mountains. According to our data, the increase in D_L ($P < 0.05$) on the 5th day in the 2d group of subjects could be attributed to increase of V_C ($P > 0.05$) under the influence of brief respiration of a hypoxic mixture. By the 15th day, against the background of maximum increase of V_C , we observed an increase in D_M diffusion resistance ($P > 0.05$) which was related to maximum resistance to diffusion of gases through the membrane. The high resistance of the alveolocapillary membrane at this stage of the experiment is probably related to residual

signs of perivascular edema [10]. In the recovery period, in tests made on the 5th and 7th days, we observed gradual decrease of D_L , which was apparently due to signs of readaptation after discontinuing the daily sessions of respiration of the hypoxic mixture, secondary changes in pulmonary blood flow and ventilation--blood flow ratio.



Dynamics of diffusion capacity of the lungs (D_L), capillary (V_C) and membrane (D_M) components. Solid lines: D_L , ml/min·mm Hg⁻¹; white columns: D_M , ml/min·mm Hg⁻¹; black columns; V_C , ml.

I) control

II) respiration of hypoxic mixture

Analysis of dynamics of D_L , V_C and D_M in the 1st group of subjects revealed the predominant influence of D_M on magnitude of D_L , which could be attributed to an increase in diffusion area, uniform distribution of blood flow in the lungs and change ventilation--blood flow ratio in response to a change in body position under hypokinetic conditions. It is interesting to note that, in the recovery period, testing of the 1st group of subjects on the 3d and 5th days revealed some tendency toward prevalence of V_C over D_M , although to a lesser extent than in the 2d group. Evidently, the minor increase of V_C is related primarily to a change in position of subjects in the 1st group after hypokinesia, but readaptation did not affect the magnitude of D_L .

Thus, it has been established that brief daily sessions of respiration of a hypoxic gas mixture under hypokinetic conditions are associated with more marked changes in D_L during the first half of the 49-day experiment. Signs of D_L adaptation in this group were observed 10 days earlier than in the control. Analysis of D_L dynamics under hypokinetic conditions in the 2d group of subjects revealed the predominant influence of V_C , whereas in the control group this applied to D_M .

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EFFECT OF DIOXANE ON FUNCTIONAL STATE OF THE RAT'S CENTRAL NERVOUS SYSTEM

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No 2, 1977 pp 87-89

[Article by G. I. Solomin, submitted 2 Dec 74]

[Text] Among the numerous chemicals, the fumes of which are demonstrable in the air of pressure chambers, there are often agents that are used as solvents in the production of polymers used in construction. According to previously published data [6], the concentrations of such agents in the atmosphere of a spacecraft, and in particular of dioxane, could reach significant levels (up to 10 mg/m^3). For this reason, the above compounds must be submitted to toxicological evaluation in order to substantiate maximum permissible concentrations thereof in the air of hermetically sealed objects.

In our experiments, we made a toxicological study of dioxane-1,4. This agent, like many other solvents, has a narcotic action; it is used widely in industry in the production of the most diverse polymer construction materials.

Our objective was to determine the nature of the effect of this compound on functional state of the central nervous system, in concentrations that could be encountered under real conditions, and to substantiate, on the basis of these tests, the threshold concentration.

Methods

The tests were conducted on 32 white rats exposed to continuous inhalation of dioxane fumes for 3 months. The animals were divided into four different groups. They were exposed to 3 concentrations of this agent: 20 mg/m^3 (1st group), 4 mg/m^3 (2d group) and 0.5 mg/m^3 (3d group). The 4th served as a control group.

We did not select these concentrations of dioxane by chance; they were determined by degree of its toxicity and need to determine threshold and subliminal concentrations, with regard to biological effects, as well as levels thereof in the air of sealed chambers. It was difficult to make the choice

of concentrations, because there are absolutely no data in the literature concerning the effects of small concentrations of dioxane on the human and animal organism in the case of long-term inhalation thereof.

In the course of our chronic experiment, the air in the test chambers was periodically analyzed for dioxane content. In addition, we took air samples from all the chambers, including the control, to analyze the products of vital functions. Air samples were analyzed on a PAY chromatograph.

As shown by the results of studies of the air environment in the chambers with the animals, the fluctuations of dioxane concentrations were negligible, and their arithmetic means coincided with the preset levels. Thus, the concentrations constituted $20.5 \pm 1.0 \text{ mg/m}^3$ in the 1st chamber, $4.6 \pm 0.3 \text{ mg/m}^3$ in the 2d and $0.54 \pm 0.005 \text{ mg/m}^3$ in the 3d. There was no accumulation of products of vital functions, since they were exposed to the agent by the dynamic method, with 4-fold exchange of air in the chamber (0.8 m^3) per hour. The parameters of the microclimate remained satisfactory throughout the experiment. The air temperature ranged from 19 to 23° and relative humidity constituted 60-70%.

We evaluated the functional state of the central nervous system according to changes in motor chronaxy of antagonist muscles and magnitude of the coefficient of correlation between extensors and flexors. It is a known fact that chronaxy of extensors is higher than that of flexors, and that the coefficient of correlation is greater than one. This ratio can change under the influence of exogenous factors, with either approximation or, occasionally, inversion. This phenomenon is interpreted as weakening of subordinational influence of the central nervous system, due to development of an inhibitory process in the cerebral cortex. In selecting this test to investigate the nature of resorptive effects of relatively low concentrations of dioxane on the animal organism, we proceeded from the thesis that the effect of threshold concentrations of toxic agents consists of general, nonspecific reactions. As a rule, these changes are functional, and they should be interpreted as defense and adaptation reactions [2].

We studied chronaxy of antagonist muscles of the right hind leg of the rats every 20 days, using the conventional method, with an ISE-01 pulsed electronic stimulator.

Results and Discussion

The data obtained on the animals are submitted in Tables 1 and 2, and the Figure. The following conclusion can be derived from the submitted results: In all groups of experimental animals, in the course of exposure to dioxane, the rheobase level did not change, in relation to background and control levels. The rheobase fluctuations for extensors constituted 3.8 to 4.5 V, and for flexors, 3.0 to 3.8 V. Statistical processing of the results by the small sample method showed that the changes obtained were unreliable.

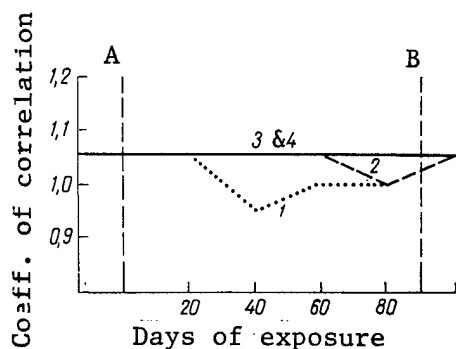
Table 1. Indices of antagonist muscle rheobase ($M \pm m$), V

Animal group	Dioxane concent mg/m ³	Muscles	Background	Days of exposure				Recovery period (10th day)
				20	40	60	80	
1	20	Extensors	3,8±0,20	4,2±0,23	4,5±0,12	4,3±0,12	4,4±0,18	3,8±0,35
		Flexors	3,1±0,20	3,6±0,23	3,6±0,18	3,6±0,18	3,8±0,28	3,1±0,35
2	4	Extensors	3,9±0,26	4,3±0,40	4,2±0,19	4,2±0,12	4,2±0,18	4,0±0,35
		Flexors	3,4±0,13	3,6±0,40	3,6±0,19	4,2±0,18	3,6±0,18	3,0±0,35
3	0,5	Extensors	4,0±0,12	4,1±0,26	4,0±0,12	4,0±0,24	4,0±0,36	4,0±0,35
		Flexors	3,2±0,24	3,5±0,26	3,2±0,24	3,1±0,24	3,0±0,36	3,0±0,35
4	Control	Extensors	4,3±0,26	4,2±0,26	4,3±0,24	4,0±0,24	4,0±0,54	3,7±0,35
		Flexors	3,2±0,20	3,6±0,20	3,2±0,24	3,2±0,24	3,0±0,36	3,0±0,35

Table 2. Indices of chronaxy of antagonist muscles ($M \pm m$), ms

Animal group	Concent mg/m ³	Muscles	Background	Days of exposure				Recovery period (10th day)
				20	40	60	80	
1	20	Extens.	0,341±0,003	0,341±0,005	0,191±0,010*	0,365±0,003*	0,370±0,004*	0,326±0,009
		Flex.	0,320±0,008	0,320±0,005	0,201±0,006*	0,360±0,004*	0,370±0,005*	0,306±0,009
2	4	Extens.	0,335±0,003	0,335±0,005	0,335±0,010	0,263±0,009*	0,260±0,010*	0,326±0,006
		Flex.	0,317±0,003	0,320±0,004	0,312±0,005	0,243±0,009*	0,260±0,013*	0,310±0,004
3	0,5	Extens.	0,340±0,010	0,348±0,008	0,340±0,010	0,338±0,005	0,330±0,009	0,325±0,010
		Flex.	0,322±0,008	0,331±0,005	0,320±0,008	0,318±0,008	0,312±0,009	0,310±0,011
4	Control	Extens.	0,341±0,008	0,341±0,005	0,341±0,008	0,334±0,005	0,330±0,007	0,333±0,007
		Flex.	0,325±0,008	0,325±0,006	0,324±0,008	0,315±0,005	0,311±0,007	0,310±0,007

* $P < 0,001$.



Correlation between chronaxy of antagonist muscles with exposure of rats to dioxane

1-3) 20, 4 and 0.5 mg/m³, respectively, of dioxane
AB) exposure period

As for chronaxy of antagonist muscles, it was sharply decreased in the 1st group of animals (20 mg/m³) already in the first half of the dioxane inhalation period, and as shown by examination of experimental animals, by the 40th day it constituted 0.191 ms for extensors and 0.201 ms for flexors. As a result of these changes, there was an inversion of normal correlation between chronaxies. The coefficient of correlation was 0.95. Thereafter, as exposure time increased, we observed an increase in reaction time, in response to electrical stimulation. On the 60th experimental day, the chronaxy of extensors constituted 0.360 ms. The high indices of chronaxy persisted to the end of the experiment, and we observed normalization of the excitatory process only on the 10th day of the recovery period.

In the 2d group of animals (4 mg/m³), we also noted changes in this index during the exposure period. However, they appeared toward the end of the experiment, and they were characterized by a decrease in reflex reaction time, which led to approximation of chronaxy levels.

In the 3d group (0.5 mg/m³), excitability of antagonist muscles remained at the same level and did not affect the chronaxy level.

All of the digital data pertaining to motor chronaxy were submitted to processing by the rules of variation statistics. The demonstrated changes in indices for the 1st and 2d groups were highly reliable ($P < 0.001$).

The results of studies of motor chronaxy in the experimental groups of animals exposed to different concentrations of dioxane enabled us to define the nature of the effect of this agent on the functional state of the nervous system, namely, to establish that there are changes in excitability of the neuromuscular system. The severity and direction of these changes are related to the inhaled concentration and time of exposure. Relatively high concentrations of this agent elicit a decrease in excitability of the neuromuscular system, while threshold levels, according to biological effect, lead, on the contrary, to increased excitability of these elements. In both instances, the changes are due to a decrease in subordinational influence of the central nervous system.

The experimental data obtained enabled us to make a toxicological evaluation of the tested concentrations of dioxane, and to define the threshold concentration in this test. It was found to constitute 4 mg/m³.

The results of experiments dealing with motor chronaxy are consistent with data in the literature [1, 3, 4], and they warrant the assumption that, when inhaled in relatively low concentrations, agents with narcotic action elicit changes in excitability of the neuromuscular system, due to the influence of the cerebral cortex. This conclusion is of great practical significance in evaluating the combined effects of toxic agents with unidirectional action, as related to determination of maximum allowable concentrations thereof in the air of sealed objects.

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CURRENT EVENTS

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SYMPOSIUM ON THE PROBLEM OF TRAINING PHYSICIANS AND SCIENTIFIC PERSONNEL SPECIALIZING IN AVIATION MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1977 p 90

[Article by G. L. Komendantov and V. I. Kopanev]

[Text] A symposium convened on 21 and 211 June 1975 in Leningrad, dealing with the problem of training specialists in the field of aviation medicine. The symposium was convened to implement the work plan of the Moscow and Leningrad sections of aerospace medicine of the All-Union Physiological Society. The staff of the chair of aviation medicine, Central Institute for Advanced Training of Physicians (TsOLIUv) and Military Medical Academy imeni S. M. Kirov (VMOLA), as well as representatives from other institutions participated in the symposium.

The main questions of the agenda of the symposium were: present status of specialist training; types of training; forms of specialization and advanced training; scientific organization of the educational process; methods of evaluating the efficacy of the pedagogical process; scientific forecast of development of aviation medicine and the pedagogical process; system of orders for training physicians and research personnel.

In the 2 days, 12 papers dealing with questions on the agenda were delivered and discussed.

The introductory paper of Prof G. L. KOMENDANTOV discussed the present status and prospects of training physicians and research specialists in aviation medicine. The paper of Prof V. I. KOPANEV dealt with evaluation of the role of lectures in training and advancement of physicians specializing in aviation and space medicine. Some important issues of methodology of instruction in aviation medicine were discussed in the paper of P. V. OBLANENKO. N. A. RAZSOLOV shared the practical knowhow on the chair of TsOLIUv with reference to educational games using stories, which permit evaluation of theoretical knowledge and practical skills in the field of medicine that deals with emergencies [and/or accidents]. The paper of O. Yu. SIDOROV discussed scientific methods of pedagogical control used by the chair of VMOLA, the effectiveness and flaws of these methods. K. A. PIMENOVA

told about the work done on the chair of TsOLIUV in the field of forecasting development of aviation medicine and use of such forecasts to upgrade the pedagogical process. The papers of E. V. BONDAREV and S. A. KLYUYEVA, V. N. RAZSUDOV and V. D. YUSTOVA devoted much attention to scientific organization of the pedagogical process, programmed testing [control] of knowledge, prospects of preparing students before series of studies and other important questions. M. D. DRAGUZYA shared the knowhow of the chair of VMOLA concerning internships in aviation practice. An extremely interesting question was raised in the paper of G. E. YEFIMENKO concerning methods of inculcating love for the profession of aviation physician.

Professors M. P. BRESTKIN, A. A. SERGEYEV, G. L. KOMENDANTOV, V. I. KOPANEV, V. P. ZAGRYADSKIY, I. N. CHERNYAKOV, I. A. PEYMER and chair instructors participated in a lively discussion.

The symposium participants expressed the unanimous opinion that such symposiums are quite beneficial to upgrading the pedagogical process on the chairs, and deemed it purposeful to hold analogous symposiums annually, with restriction of the range of issues to be discussed. Furthermore, it was deemed useful for the chair of TsOLIUV to assimilate the knowhow of VMOLA with regard to internships for students in aviation practice, and for the VMOLA chair to adopt the knowhow of the TsOLIUV chair with regard to educational gains, using stories [legends] in classes on the area of aviation medicine that deals with emergencies. For this purpose, it was deemed purposeful to practice temporary exchange of instructors. The opinion was voiced that it would be expedient to exchange instructors to deliver some of the lectures. Approval was expressed of the existing practice of exchange of educational aids, syllabuses and other material of the chairs.

This symposium on upgrading the pedagogical process, organized for the first time by the chairs of TsOLIUV and VMOLA in accordance with the plan of the Moscow and Leningrad sections of aerospace medicine of the All-Union Society of Physiologists, showed its great effectiveness and timeliness. Furthermore, the symposium formulated the task of upgrading the pedagogical process to conform with the distinctions of scientific and technological progress.

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